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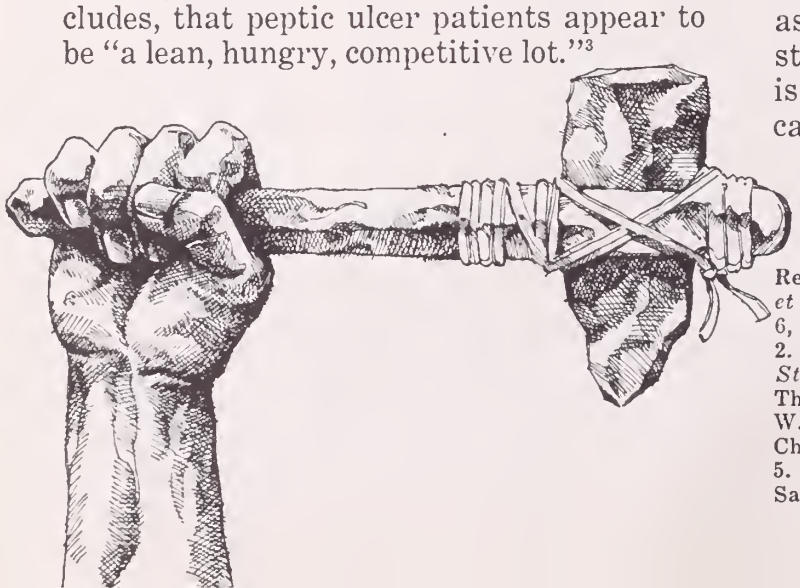
IF MORE MEN CRIE



At least seventy-five out of one hundred adults with duodenal ulcers are men.[1] Why? It may be significant that duodenal ulcer patients tend to crave recognition and are "especially vulnerable to threats to their manly assertive independence."[2]

Hypersecretion—an atavistic response. Stewart Wolf, who, with Harold G. Wolff, studied the personalities of duodenal ulcer patients, wonders if masculine competitiveness is related to "an atavistic urge to devour an adversary." It is striking, he reports, that an accentuation of gastric acid secretion and motility can be "induced in ulcer patients by discussions that arouse feelings of inadequacy, frustration and resentment."[2]

By chance? A lean, hungry lot. Was the link between emotions and gastric hyperacidity acquired through mutation to serve a purpose? During man's jungle period of evolution, the investigator points out, a male dealt with a foe by killing and devouring it. "It may be more than coincidence," he concludes, that peptic ulcer patients appear to be "a lean, hungry, competitive lot."[3]



Big boys don't cry. If more men cr maybe fewer would wind up with duode ulcers. But men will be men—the sum tota their genes and what t are taught. Schottst observes that whe mother admonishes son who has hurt him that big boys don't cry, is teaching stoicism.[4] Crying is negation of everyth society thinks of as ma A boy starts defending manhood at an early

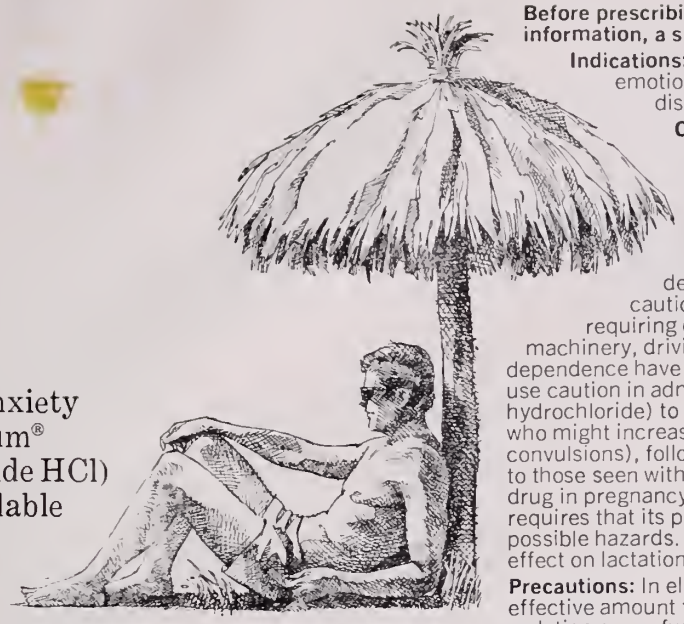


Take away str you can take away sympto

There is no question that stress play role in the etiology of duodenal ul Alvarez[5] observes that many a man with ulcer loses his symptoms the day he shuts the office and starts out on a vacation. problem is, the type of man likely to have ulcer is the type least likely to take l vacations or take it easy at work.

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References: 1. Silen, W.: "Peptic Ulcer," in Wintrobe, M *et al.* (eds.): *Harrison's Principles of Internal Medicin* 6, New York, McGraw-Hill Book Company, 1970, p. 2. Wolf, S., and Goodell, H. (eds.): *Harold G. W Stress and Disease*, ed. 2, Springfield, Ill., Charl Thomas, 1968, pp. 68-69. 3. *Ibid.*, p. 257. 4. Schottst W. W.: *Psychophysiologic Approach in Medical Pra* Chicago, Ill., The Year Book Publishers, Inc., 1960, p. 5. Alvarez, W. C.: *The Neuroses*, Philadelphia, Pa., W Saunders Company, 1951, p. 384.



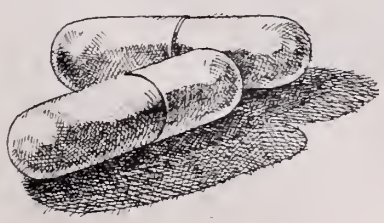
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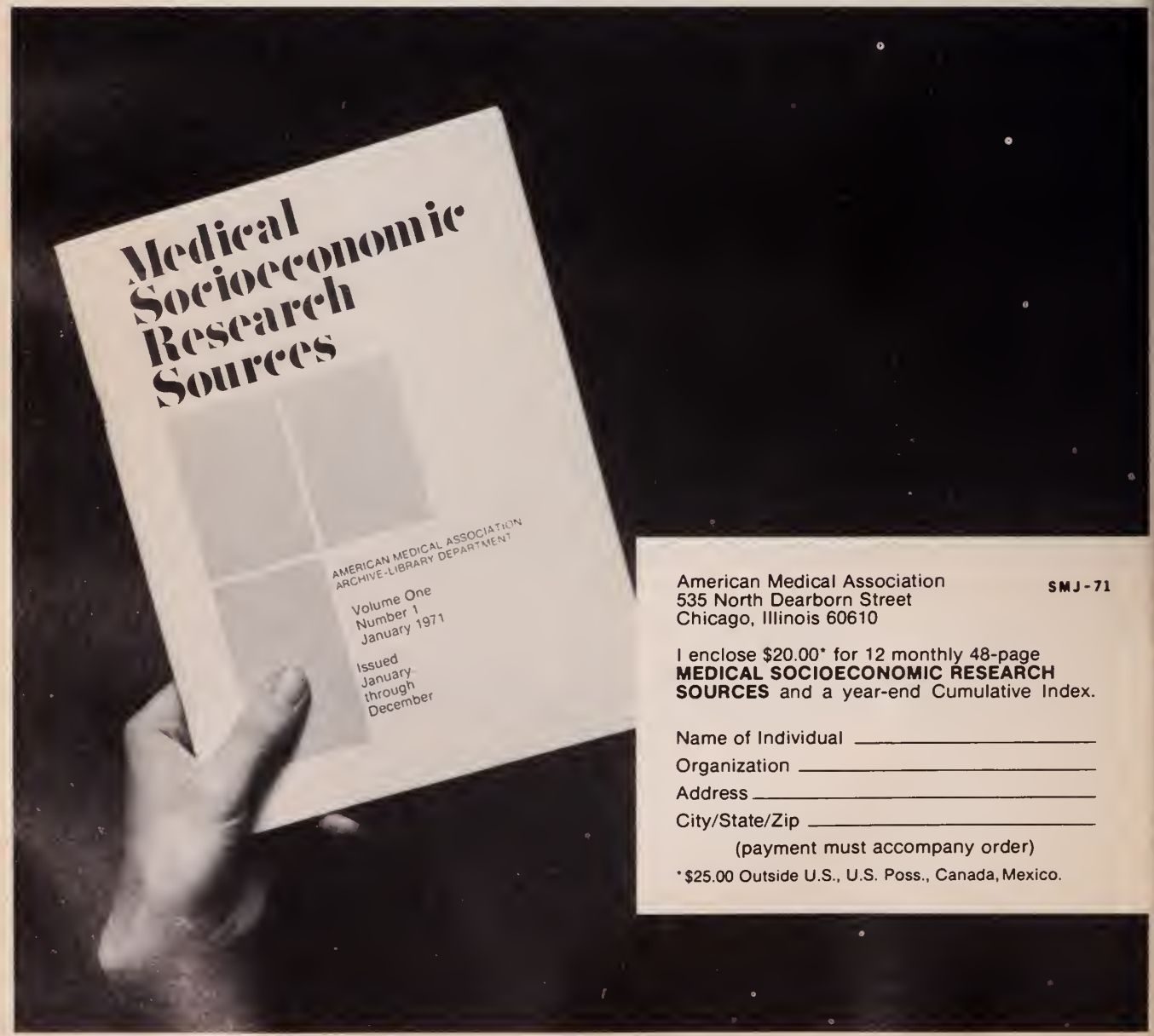
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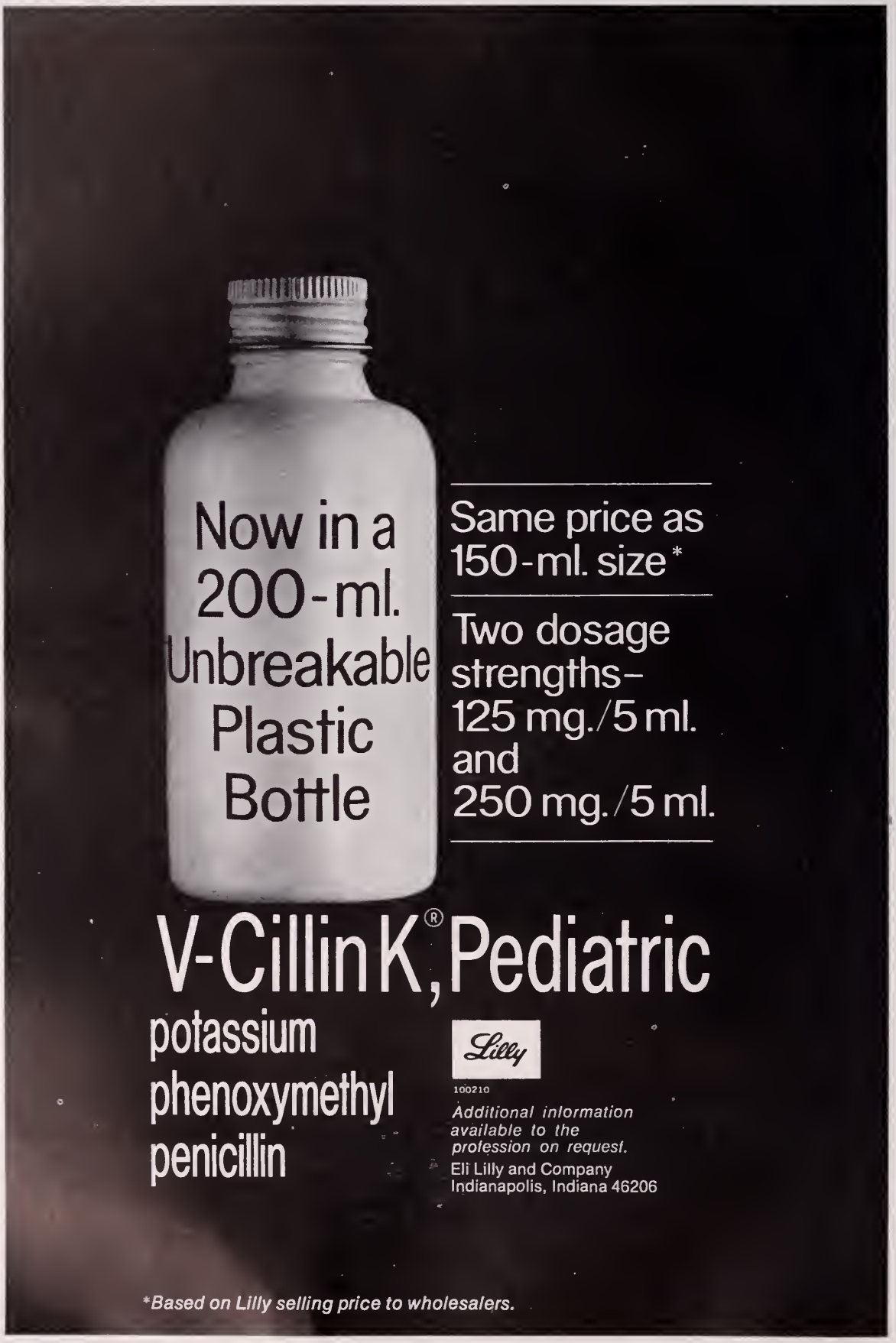
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Treatments and diagnostic studies requiring special equipment and trained assistants; no liability* and no determination of need—$3.00 per treatment or study plus the pro-rated hourly wage of assistant. With liability and determination of need—$9.00 per treatment or study plus three times the pro-rated hourly wage of assistant.

Travel of owner and proprietor in his own vehicle to make any of the above commodities available to an individual purchaser—$0.50 per mile or any portion of mile.

- Services and commodities not shown above will require negotiated fees.
- Fees shown apply only to direct cash payments made by purchaser at time of purchase. Deferred payments by purchaser or third party must be negotiated and will require payment of lawful interest as described in the documents executed at the time of negotiation.
- Approved credit cards are accepted.
- Our rock-bottom prices prohibit the award of trading stamps.
- Ask any of our sales ladies about our exciting 'discount plan' for groups of 100 or more. It eliminates the fancy but expensive 'freedom of choice' and 'personal service' concepts. A *real* saving!—*MRJ* □



Your House of Delegates met in special session on December 12th, 1971, and ratified two resolutions presented by the Board of Trustees, one concerned with Peer Review and the other with Blue Shield relations. The former was passed unanimously and the latter with less than five (5) dissenting votes. This meeting was an excellent demonstration of our democratic process with forceful deliberation devoid of emotionalism. Who knows, but that the action of this House may be viewed in the future as an important event in Oklahoma medicine.

Peer Review may not become operable until Congress has passed the National Health Insurance Bill, which promises to be a major issue in the '72 presidential campaign. In my opinion, this action of the House of Delegates demonstrated its wisdom and its desire to keep pace with changing times.

The withdrawal of the medical society's endorsement of Blue Shield and Blue Cross, I hope, will remove obstacles which in recent years have prevented an amicable association for the best interest of the patient, organized medicine and voluntary prepaid health insurance. The future of private third party payers and the private practice of medicine is in considerable jeopardy, and we can ill-afford a recurrence of a confrontation such as we have recently experienced.

The Oklahoma legislature has reconvened. The time is now for physicians to support our Legislative Committee chaired by R. Barton Carl, M.D., and David Bickham representing our headquarters staff. These people have rendered yeoman service in the past but we cannot expect them to continue to shoulder a load which we should all share.

Physicians of the future, though concerned with primary care of the patient, must broaden their field of activity. The delivery of health care not only involves actual contact with the patient, but necessitates participation in socio-economic fields and cooperation with governmental (federal, state, county and city) agencies and organizations in addition to non-governmental groups representing society, health, labor, business and insurance, just to name a few.

Having in the last few months heard speeches by Congressman Jack T. Broyhill of Virginia, Senator Russell B. Long of Louisiana and Vice-President Spiro Agnew, any doubt existing in my mind regarding National Health Insurance has been dispelled. It is only a matter of time before we have it. Once here, one can only speculate as to further developments down the road. The future of medicine and the welfare of the patient and practitioner may well depend on the role of the physician in politics. It is imperative, that those of our colleagues who are inclined toward politics become more active, even though it may involve self-sacrifice.

Those of us who shun the atmosphere of politics can nevertheless play a small part in fashioning medical practice of the future. I would suggest more frequent contact with our legislators reminding them of our thoughts and concerns, more political motivation and participation in diverse legislative matters, service as "Physician of the Day" during the legislative sessions, and personal financial contributions to our legislators and would-be legislators. Daily indoctrination of our patients for our mutual welfare in legislative concerns is emphasized.

Since it is not likely that as a state society we can obtain the expertise or the finances for extensive lobbying, we should contribute to OMPAC (Oklahoma Medical Political Action Committee) locally which in turn contributes to AMPAC (American Medical Political Action Committee). The benefits to physicians accruing from these two organizations are very much underestimated.

Sincerest wishes to all for satisfaction and success during the year '72. □

Sincerely,

Lucien H. Pascuzzi

OSMA JOURNAL/scientific

Image Enhancement in Nuclear Medicine

DAVID S. GOODEN, Ph.D.
CHARLES H. FARMER, Ph.D.
JOHN E. KAUTH, M.D.

The nuclear medicine image is inherently of poor resolution. Computerized image enhancement shows real promise in providing the physician with images with significantly improved detail.

SELDOM IN THE history of medical science has a discipline shown such spectacular growth as nuclear medicine. Since its early beginning, shortly before World War II, when artificially produced radionuclides first became available we have seen nuclear medicine develop into one of the most exciting and important components in modern biomedical science.

Nuclear medicine has developed in two categories. The first is *in vitro* studies which provide information on system physiology by measuring constituents of the blood and other body fluids. The second is *in vivo* studies which are used primarily for imaging internal structures and providing dynamic information.

Although nuclear medicine imaging has become an important diagnostic tool for medicine, the images themselves have intrinsically poor resolution qualities. It is unlikely that significant improvements will be made in instrument resolution in the near future. The very nature of the "object plane" being viewed accounts largely for the poor quality images. Computerized image enhancement, however, appears to hold real promise in providing the clinician with nuclear medicine images which have been significantly improved in diagnostic value.

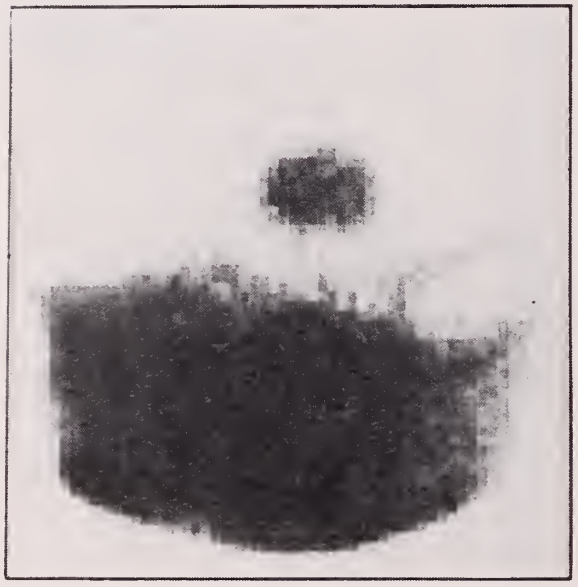
The term enhancement is used here to mean a subjective improvement of the apparent quality of the image; that is, the result should be an image from which the clinician can extract either more diagnostic information or the same information faster or easier. Enhancement of an image requires that the image portions bearing diagnostic information be maintained while diagnostically unimportant portions are reduced. Enhancement can be implemented in several different forms; for example, an image can be improved by matching its properties better to the properties of the eye, by compensating for known instrumentation degradations in the system which recorded the original image, or by determining the diagnostically important characteristics of the images and designing a system to preferentially amplify these characteristics.

EQUIPMENT

Although we do not wish to discuss spe-

From St. Francis Hospital and William K. Warren Medical Research Center, Tulsa, Oklahoma 74136.

cific hardware or software systems, it may be useful to mention some of the physical components necessary for picture processing. For most of the work being done today a digital computer functions as the heart of the system. Since the computer works with numbers, the first step in picture processing is to represent the image by a group of numbers. In nuclear medicine this can be done in two ways. The first is with "on-line" techniques which actually store an array of numbers within the computer memory as the picture is being taken. The second is with "off-line" techniques in which an image is scanned by a device similar to a television camera. The resultant electrical signals, representing the brightness of successive image elements, are changed by an analog-to-digital converter into numbers which are stored on computer compatible magnetic tape. This operation provides a numerical version of the input image which can then be processed by the computer. Methods of displaying the resultant image after computer processing can also be accomplished by both "on-line" and "off-line" techniques.



ORIGINAL IMAGE



FILTERED IMAGE

Figure 1. Original and enhanced scan.

APPROACHES

Let us now return to the question of how we go about making an image better. If we had a unique criterion of image quality, we

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would optimize that quality criterion. Unfortunately, the status of image-quality research in the biomedical sciences is not such as to provide us with this answer at this time. Therefore, we must proceed on a somewhat intuitive basis and, as might be expected there are several different approaches to the problem. All approaches essentially try to improve the clinically significant information and/or reduce the noise level in the enhanced image.

Matching the Eye Response

One may look at an image and quickly make an evaluation such as normal or abnormal, pretty or ugly, art or junk. However, neither the psychology nor the physiology of the human visual system is a well understood phenomenon. Certainly the evaluation process used is not defined well enough to be machine implementable. One reason is the "semantic" content of an image varies with each individual. Also, typical of most clinicians, a set of comparative images is in the memory of human observers. That is, the evaluation is relative both to the image and to the observer.

Correction of Imaging Systems

Turning to correction for instrumentation deficiencies, we have an area where the bulk of the research has been concentrated. In order to characterize the effect of a system on an image, many researchers make the rather gross assumption that the operation on the image by the system is both linear and position invariant.

1) Linearity is distinguished by two basic properties:
   a) the output corresponding to a sum of inputs is equal to the sum of the outputs corresponding to the inputs acting separately; and
   b) multiplication of the input by a constant multiplies the output by the same constant.

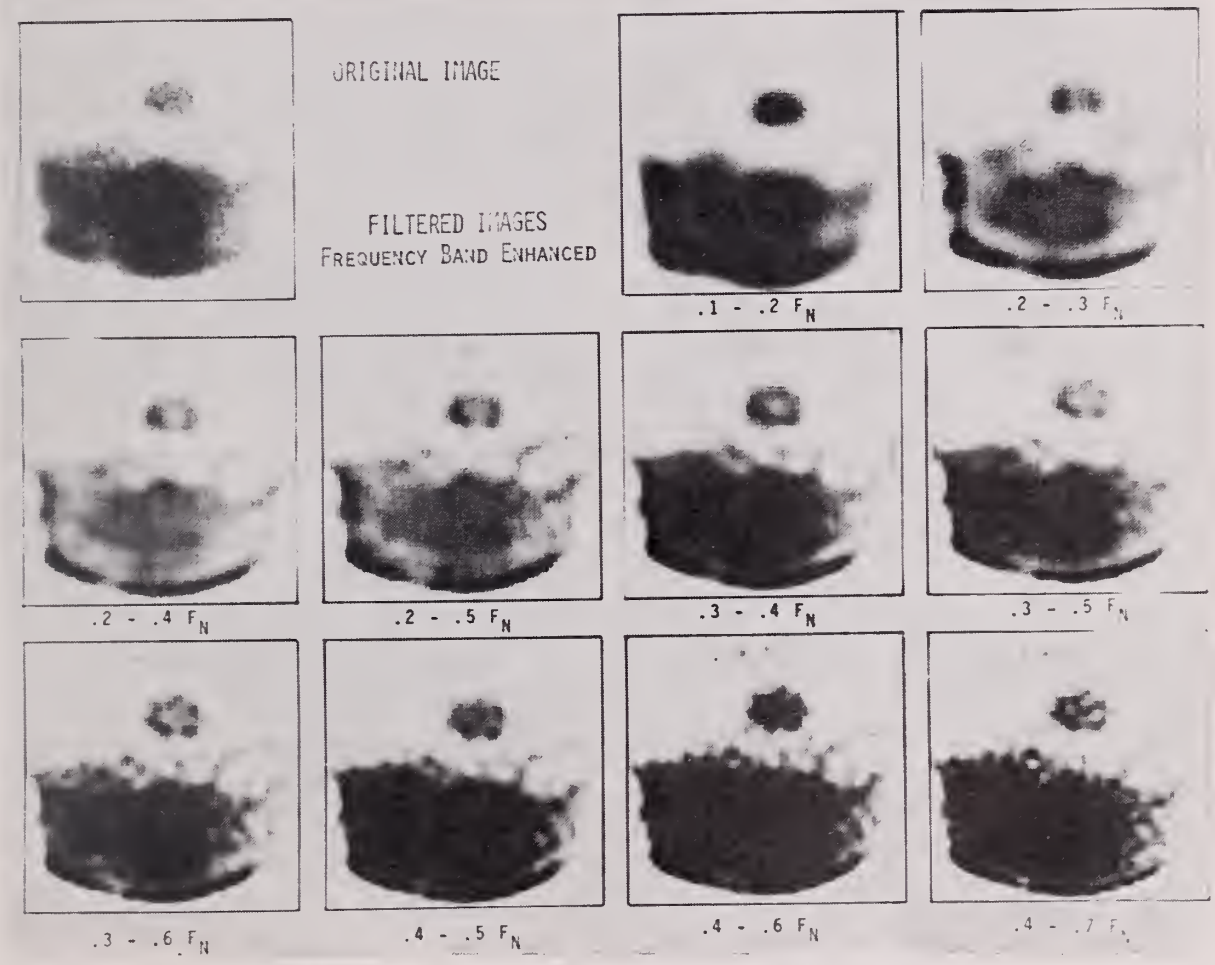


Figure 2. Enhanced images using various cut-off frequencies

2) Invariances require that the image of a point does not depend on the original position of the point.

It is often convenient to describe the operation by the imaging system in terms of its effect on simple input pictures, e.g., pictures which have zero intensity except at the points of a straight line. The response of an imaging system acting on such a picture is called *line spread function.*

Still another common method of describing the response of an imaging system is recording its effect on a sinusoidal input picture. The entities that describe this effect as a function of the spatial frequency of the input sinusoid are called the *Modulation Transfer Function* and *phase transfer function* respectively. These functions are mathematically the amplitude and phase of a function which is obtained by performing what is known as a Fourier transform of the line spread function. The Fourier transform is a mathematical technique which allows an image to be represented by sinusoidal components of different amplitudes and frequencies. Image processing is often more easily implemented in the frequency domain.

If we now know how the imaging system responds to various sinusoidal components (Modulation Transfer Function) and the sinusoidal composition of the original image (Fourier transform) we can correct for any system degradations. To date, this has been the most common approach to image enhancement in nuclear medicine. It has been shown recently in research conducted at St. Francis Hospital that this may not be the most fruitful approach.

Frequency Band Enhancement

Our image enhancement technique has been designed by carefully studying the nature of the sinusoidal composition of nuclear medicine images. We have designed filters which preferentially amplify that portion of the sinusoids which carry information of diagnostic value. We have coined the phrase "frequency band enhancement" to describe this technique. Figure 1 shows an observed scan as obtained with a Nuclear Chicago Pho Gamma camera and a scan which has been enhanced using a band enhancement filter. The enhanced image shows a "cold core" within a tumor. Surgical samples show a totally necrotic center within the tumor which confirmed the "cold core" seen on the scan. The enhanced images also provide superior definition in regions of the transverse sinus and the pituitary fossa. Figure 2 shows a number of enhanced images. All enhancement was done with band enhancement filters, but with various frequencies of interest amplified.

SUMMARY

There is, of course, much that needs to be done in the implementation of image enhancement in nuclear medicine. It must be made to be of diagnostic value to the physician. It must also be reasonably economical to gain wide acceptance. With an application as novel as image enhancement in nuclear medicine it is naive to say that a given method has all the advantages; however, "frequency band enhancement" filtering certainly appears to hold promise in providing the images of improved diagnostic values which are so important in nuclear medicine today. Results of this research are being reported nationally. We are pleased that what we consider to be a significant contribution to this area was made in the state of Oklahoma. □

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The Use of the Doppler Ultrasonic Flowmeter During Myocardial Revascularization

(A Preliminary Report)

E. L. LICHTI, Ph.D.
AHMED ELKADI, M.D.
C. H. ALMOND, M.D.

The Doppler Ultrasonic Flowmeter may be used at operation to determine the patency and approximate flowrate in the saphenous vein graft used for revascularization of the myocardium.

IN MYOCARDIAL revascularization procedures using a vein bypass graft, it is necessary to determine the patency of and the approximate flowrate through the graft. While the electromagnetic flowmeter indicates only the flowrate, the Doppler ultrasonic flowmeter gives a wider range of information including the approximate flowrate and the flow pattern in the graft, and the condition of the peripheral coronary vascular bed. The Doppler method is also simple, reliable, and absolutely atraumatic.

In 1961 Franklin, *et al.*[1] described an ultrasonic flowmeter which utilized the Doppler effect as a useful tool in the determination of bloodflow in animals. The feasibility of determining intravascular, pulsatile bloodflow transcutaneously was later demonstrated.[2] Peripheral vascular occlusive disease evaluation with the Doppler has been documented by Strandness, *et al.*[3] Keitzer, Lichti, and DeWeese[4] reported on the use of the ultrasonic flowmeter during vascular reconstruction for arterial occlusive disease. Elkadi, *et al.*[5] use the Doppler for the pre- and postoperative evaluation of cannulation sites for cardiopulmonary bypass. With the advent of the directional Doppler, the operator may now read out the frequency shift (f_d) of intravascular bloodflow and determine the direction of flow and velocity of blood in a particular vessel. It is the intent of this communication to present a simple means of ascertaining the patency of a saphenous vein graft, used for myo-

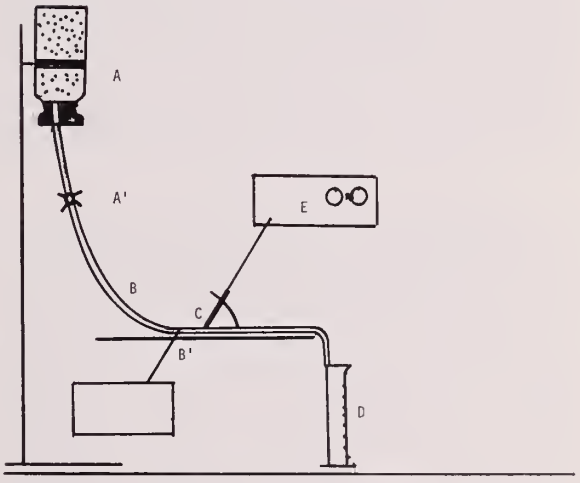


Figure 1. Schematic Diagram of Apparatus Used for Comparative Flowrate Study with the Doppler Ultrasonic Flowmeter, Electromagnetic Flowmeter, and Volumetric Measurement. (A—Blood Sample, A′—Stopcock for flow control, B—2 mmID silastic tubing, B′—Electromagnetic flowmeter, C—Doppler probe at 60° angle to silastic tubing, D—Volumetric graduate, E—Model 806 Directional Doppler.)

From the University of Missouri School of Medicine, Department of Surgery, Columbia, Missouri.

Table 1
DOPPLER FLOW RATES COMPARED WITH VOLUMETRIC MEASUREMENTS

Test	Flow Rate (ml/min.) Doppler	Volumetric
1.	150	155
2.	97	90
3.	120	135
4.	53	48
5.	148	148
6.	127	115
7.	15	15
8.	180	180
9.	150	160
10.	100	110

cardial revascularization, at operation and semiquantitatively determine flowrate through the graft.

METHODOLOGY

The frequency shift noted with the directional Doppler flowmeter, Model 806, is directly correlatable with the velocity of bloodflow in the vessel. Utilizing the formula of Wolff,[6] $Q = f_d\ (d)^2\ (1.414) \times 10^{-2}$, where Q is the flow rate, f_d the frequency shift in cycles per second, and d the diameter of the vessel in millimeters when multiplied by 1.414×10^{-2}, the flowrate in a given vessel may be calculated within the theoretical limits of the accuracy of the aforementioned equation.

To evaluate the efficacy of the formula a simple experiment was designed and apparatus assembled in the laboratory for a controlled volumetric comparison (Figure 1). The device consisted of an IV bottle (A) filled with whole blood and a stopcock (A′) connected with a 2mm internal diameter section of silastic tubing (B) where flow is detected with a Doppler probe mounted at an angle of 60° to the tubing. The blood whose flow is controlled by the stopcock at A′ was collected for specific time intervals and Doppler flowrates, according to the equation, were calculated and compared to volumetric flow. These data are presented in Table 1. The experiment was repeated with a square wave electromagnetic flowmeter in position

Table 2
DOPPLER FLOW RATES COMPARED WITH ELECTROMAGNETIC FLOWMETER AND VOLUMETRIC MEASUREMENTS

Test	Flow Rates (ml/min.) Electromagnetic Flowmeter	Doppler	Volumetric
1.	95	115	110
2.	105	115	105
3.	95	75	75
4.	95	95	70
5.	120	115	95
6.	165	160	150
7.	130	150	135
8.	150	140	135
9.	30	25	20
10.	160	180	165



Figure 2. Saphenous Vein Graft for Myocardial Revascularization.

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B′ of Figure 1. Flowrate data from the electromagnetic flowmeter, ultrasonic flowmeter, and by volumetric measurement are presented in Table 2.

RESULTS

The data presented in Table 1 compare Doppler calculated flowrates with volumetric measurement of flow. In ten runs there is an average deviation of ±5.895 percent in comparison of Doppler flowrate with volumetric measurement. Maximum positive deviation was 10.43 percent and maximum negative deviation was 11.11 percent. Air bubbles in the blood caused rapid, transitory shifts in the f_d thus introducing some error into the calculated flowrate determined by Doppler. Unfortunately, in the system used the extraneous air bubbles could not be avoided.

In the repeat experiment more error was introduced because the blood was filtered prior to the runs and more air was introduced. In Table 2 it is noted that there is an average deviation of ±12.65 percent when comparing the Doppler calculated flowrate to the volumetrically measured flow. The electromagnetic flowmeter rates showed an average deviation of ±18.00 percent from the volumetrically measured flow. The Doppler calculated flowrates have a positive maximum deviation of 35.70 percent in comparison to the volumetrically measured flow and no negative deviation was noted. The electromagnetic flowmeter had a maximum positive deviation of 50.00 percent and a maximum negative deviation of 13.60 percent.



Figure 3. Ascertaining Patency and Flowrate Through Aorta-Coronary Artery Bypass Graft with Doppler Ultrasonic Flowmeter.

CLINICAL APPLICATION

The vein graft, which connects the aorta to one or more of the coronary arteries is examined with a gas sterilized Doppler probe to ensure its patency. Frequency shift is read directly off the scale of the apparatus and the approximate flowrate through the graft is calculated after measuring the diameter of the graft. This procedure gives the surgeon the required information about the patency and the efficiency of the vein graft. Also, the sound quality of the Doppler indicates to some extent the flow pattern in the graft and the condition of the peripheral coronary vascular bed which affects the long term prognosis.

DISCUSSION AND SUMMARY

The purpose of this paper is to present a simple and reliable method of ascertaining patency of the vein graft used in myocardial revascularization procedures, and providing an estimation of approximate flowrate in the graft. The Doppler ultrasonic flowmeter as described herein, has been used to provide meaningful information on the hemodynamic state of the involved vasculature, without associated morbidity or mortality. Experimental evaluation and clinical application of the Doppler ultrasonic flowmeter are described. □

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Normal Values for the Radioactive Iodine Uptake and the In Vitro Thyroid Studies in Eastern Oklahoma

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D. S. GOODEN, Ph.D.
H. J. HELINSKI, R.T.N.M.
R. D. DUNLAP, R.T.N.M.

Recent reports have shown the importance of periodic checks of the normal values of radioactive iodine uptake. Ninety-two normal subjects were studied to establish new normal limits for the "thyroid uptake" and other thyroid function studies in eastern Oklahoma.

RECENT REPORTS[1, 2, 3] have shown the importance of periodic checks on the normal values of radioactive iodine uptake. These studies have shown a general decrease in the uptake of radioactive iodine in normal subjects. Pittman, *et al.*[1] have shown that the lowered uptake is due to an increase in dietary iodine and is particularly due to increased amounts of iodine in commercially prepared bread. It has also been demonstrated that it is important to establish normal values on a regional basis, since the normal limits do vary within different parts of the country. Oddie, *et al.*[4] have reported that the daily dietary intake of iodine in different sections of the United States varies from 240 to 740 micrograms.

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PROCEDURE AND RESULTS

Ninety-two (92) clinically euthyroid volunteers (52 females and 40 males) ranging in age from 18 to 60 years and living in the Tulsa, Oklahoma, area were selected from the staff of St. Francis Hospital. Each was evaluated by history and physical to exclude those with thyroid, renal or cardiac disease. Twenty-eight (28) of the women were on estrogens. No volunteers taking other medication known to affect thyroid function tests were used.

A five to ten microcurie capsule of ^{131}I (Squibb) was given to each subject and a 24 hour uptake was done, using a standard technique. In addition, blood was drawn prior to giving the capsule for determination of the T4 by column[5] and T3 and T4 by isotope. The T3 determinations were made using a resin sponge method (Abbott ^{125}I Kit) and T4 values were obtained using a Sephadex column technique (Ames ^{125}I Kit). The T7 values (free thyroxine index) were calculated from values of the T3 and T4 tests.

The mean value and the standard deviation were determined for each test. The proposed 95 percent confidence interval was established by taking the mean value ± 2 standard deviations. Individuals for the uptake study are divided into sub-categories consisting of total volunteers, volunteers on no estrogen, volunteers on estrogen, male volunteers and female volunteers (see Table 1). For the *in vitro* test only three groups

Table 1
24 HOUR RADIOIODINE UPTAKE IN NORMAL SUBJECTS

	Total	No Estrogen	Estrogen	Male	Female
Number of Subjects	92	64	28	40	52
Mean Value	14.9%	15.0%	14.5%	13.6%	16.2%
Standard Deviation	4.3	4.1	4.7	3.6	4.4
Suggested Normal Range*	6.3 - 23.5%	6.9 - 23.2%	5.1 - 13.9%	6.4 - 20.7%	7.4 - 25.1%

*Proposed 95% confidence interval (mean value ± two standard deviations).

Table 2
IN VITRO BLOOD STUDIES OF THYROID FUNCTION†

	T3 (Abbott)	T4 (Ames)	T7	T4 (By Column)
Manufacturer's Normal Range	25 - 35	3.5 - 8	2.9 - 9.2	3.2 - 6.4
Subjects (Total)*	17.3 - 32.5	2.6 - 8.5	2.7 - 6.5	2.9 - 6.8
Subjects (No Estrogen)*	20.6 - 32.6	2.7 - 7.5	2.5 - 6.1	3.0 - 6.2
Subjects (Estrogen)*	15.8 - 25.9	4.6 - 9.8	3.7 - 6.8	3.5 - 8.2

†Same subject group reported in Table 1.
*Proposed 95% confidence interval (mean value ± two standard deviations).

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H. J. Helinski, R.T.N.M., is an Instructor in the School of Nuclear Medical Technicians at St. Francis Hospital in Tulsa. He is a member of the Society of Nucelar Medicine and the Society of Nuclear Medicine Technologists.

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are reported: total volunteers, volunteers on no estrogen and volunteers on estrogen (see Table 2). The manufacturer's stated normal limits for the *in vitro* test are also shown.

DISCUSSION

The new normal range at St. Francis Hospital, Tulsa, Oklahoma, for the radioactive iodine uptake has been established to be from 6.3 to 23.5 percent. This is consistent with recent reports from Alabama,[1] California[2] and Wisconsin[3] which give normal values of 15.4 ±6.8 percent, 18 ±7 percent, and 12.1 ±6.1 percent respectively. In these studies the limits represent ±1 standard deviation only. In our study no significant relationship between radioactive iodine uptake and estrogen ingestion was noted. We did find, however, that the average uptake in males was approximately 16 percent less than the average uptake in females. This is consistent with the report of Oddie, *et al.*[4] which states that the mean iodine intake in males is 34 percent greater than in females.

In addition to the establishing of uptake normal values, local normal values were also established for *in vitro* tests for thyroid function. The results of the isotope T3 and T4 tests were particularly interesting and in all cases our established normals varied significantly from the manufacturer's stated normal limits. According to manufacturer's

stated normal values, 39 volunteers fell outside normal limits for the T3 isotope test, 11 outside normal limits for the T4 isotope test and 13 outside on the T4 by column. Alteration in thyroxine binding globulin was well demonstrated in the 28 patients using estrogens. Twenty-six (26) fell outside the manufacturer's normal limits with the T3 isotope test and seven outside normal limits on the T4 isotope test. Comparison of the proposed normal values for T7 in patients receiving no estrogens with those receiving estrogens indicated little difference. Such data suggest to us that, for the present, the best *in vitro* screening test for thyroid function is a combination of radioactive T3 and T4 with a calculated T7. □

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St. Francis Hospital, Tulsa, Oklahoma 74135

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1. Demeulenaere, L.: Action du R 1132 sur le transit gastro-intestinal, Acta gastroent. Belg. 21:674-680 (Sept.-Oct.) 1958.

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A Longitudinal Study of Medical Specialty Choice

JOHN G. BRUHN, Ph.D.
OSCAR A. PARSONS, Ph.D.

Medical students' attitudes toward medical specialties are compared with their specialty choices upon entering practice. While the majority of students entered specialties which differed from their career choices as medical students, more students who changed specialties entered technically-oriented ones, while non-changers entered person-oriented specialties. These findings were discussed with respect to the shifting emphasis toward community-oriented physicians.

THE CHARACTERISTICS of medical specialty groups, medical student attitudes toward various medical specialties and the relationship of these factors to students' projected career goals have been studied frequently. However, little attention has been given to the assessment of changes in both student attitudes toward specialties and career goals from the time of entry into medical school to taking up medical practice. It is known that specialty choices change during internship and residency and, although less frequently, after entry into practice. Few investigators have studied the process of career choice among medical students prospectively to the time they entered practice.

Yufit and his colleagues,[1,2] made predictions of specialty choices among freshmen medical students using personality tests, interest and experience questionnaires, and the ratings of observers who evaluated students' behavior during interviews with patients. Changes in student attitudes, life styles and certainty of specialty choices were assessed by questionnaire during the senior year and at three, five and seven year intervals post-graduation. Fifty-five percent of the medical students in this study made no permanent change in their specialty choice between their freshmen and senior years. Those students who were primarily technique-oriented were more accurate in their self-predictions of specialty choice,

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both as freshmen and as seniors, than students who were more person-oriented. The observers who rated freshmen students' behavior in clinical situations were more accurate in predicting students who eventually entered person-oriented specialties. The study indicated that specialty choices had become stable for 90 percent of the physicians by five years post-graduation. None of the ten percent who changed specialties after this time entered person-oriented specialties.

The present study reports comparisons between attitudinal data obtained from four classes of medical students regarding various medical specialties and their specialty choice upon entering medical practice. The specific questions investigated were: 1) How many students entered a specialty which differed from their original preference? 2) What was the original stereotype students had of the specialty they eventually entered? 3) What differences, if any, exist in the stereotyping of students who changed and who did not change specialty choices? 4) Did more students who changed specialties shift toward technical-oriented or toward person-oriented specialties?

METHODS

A questionnaire, designed by the World Federation for Mental Health, was given in 1962 to 343 students (199 pre-clinical and 144 clinical) attending the University of Oklahoma Medical School. While the questionnaire dealt with various aspects of mental health and illness, specific questions were included to elicit students' attitudes toward four medical specialties and their specialty choice at that time. Students were presented a list of ten personality traits and asked to select the one specialty, either surgery, internal medicine, psychiatry, or general practice, which they thought was most typical of each trait.[3,4] A characterization of each of the specialties was obtained for each student. During 1970, after allowing time for the freshman class of 1962 to complete internships and residencies, the specialty choices of all 343 students were sought. Through current information in alumni records and from class secretaries, the specialty choices of 88 percent or 301 of the original sample were obtained. These data were then compared with students' characterizations of the four specialties and their stated career choices while in medical school.

Table 1
STUDENTS WHO CHANGED AND WHO DID NOT CHANGE SPECIALTY CHOICE BY SPECIALTY ENTERED

	Specialty Entered: Students Who Changed Specialty Choice (N=203)		Students Who Did Not Change Specialty Choice (N=84)	
	Observed	Expected	Observed	Expected
Internal Medicine	46	46.68	20	19.32
Surgery	50	53.05	25	21.95
ENT	16	14.15	4	5.85
Psychiatry	10	10.61	5	4.39
Pediatrics	13	11.32	3	4.68
Ob-Gyn	15	12.02	2	4.98
Radiology	22	15.56	0	6.44
General Practice	31	39.61	25	16.39

$X^2 = 20.45$; 7df; $p < 0.01$

RESULTS

Changes in Specialty Choice

Two hundred and eighty-seven of the 301

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Table 2
TRAITS ASCRIBED TO FOUR MEDICAL SPECIALTIES BY STUDENTS WHO CHANGED AND STUDENTS WHO DID NOT CHANGE SPECIALTY CHOICE

	Students Who Changed Specialty Choice (N=203)*					Students Who Did Not Change Specialty Choice (N=84)*				
Traits:	Surg. %	Int. Med. %	Psych. %	G.P. %	N=	Surg. %	Int. Med. %	Psych. %	G.P. %	N=
Deeply interested in intellectual problems**	2	27	67	4	196	9	27	64	0	81
Domineering and arrogant	88	7	4	1	199	93	4	2	1	80
Emotionally unstable	15	6	74	5	193	19	5	69	7	75
Deeply interested in people***	0	4	20	76	193	5	6	16	73	80
Aggressive and full of energy	46	11	2	41	198	52	10	4	35	81
Confused thinker	8	11	67	13	186	13	6	59	22	68
Extremely patient****	4	15	32	49	195	11	21	25	43	80
Mainly concerned with own prestige	78	10	8	4	194	69	15	8	8	78
Friendly, pleasing personality	0	11	5	84	192	1	13	8	77	75
Sensitive to a wide range of factors when evaluating a medical problem*****	5	46	10	40	197	0	70	8	23	79

*Total possible N for each of the ten items. "No opinion" responses were excluded from analysis.
**$X^2 = 9.26$; 3df; $p < 0.05$
***$X^2 = 10.66$; 3df; $p < 0.02$
****$X^2 = 7.47$; 3df; $p < 0.05$
*****$X^2 = 14.74$; 3df; $p < 0.01$
Chi-squares were computed comparing students who changed vs. students who did not change specialty choice for each of the ten traits.

students had entered eight medical specialties including general practice. The remaining 14 students entered a variety of specialties. Since the numbers of students in these specialties were too small for separate analysis, these specialties were excluded from the present study.

Two hundred three or 71 percent of the 287 students (270 males, 17 females) comprising the final sample entered specialties which differed from their choices as medical students. As would be expected significantly more of the pre-clinical students changed specialties (77 percent) compared to students in the clinical years (63 percent) ($X^2 = 6.87$; 1df; $p < 0.01$).

Table 1 compares the specialty choices of students who entered and did not enter the specialty choice they had indicated as students. More students who changed specialties entered obstetrics-gynecology and radiology, while more of the non-changers entered surgery and general practice. The overall chi square between these groups was significant ($X^2 = 20.45$; 7df; $p < 0.01$).

Characterization of Specialty Entered

The characterizations of surgery, internal medicine, psychiatry and general practice were identical to those found in our initial study.[3]

Characterizations of Specialties Among Changers and Non-Changers of Specialty Choice

Table 2 shows that, while the overall characterizations of the four specialties did not differ greatly between students who changed and who did not change specialties, significantly fewer of the changers saw the surgeon as deeply interested in intellectual problems, deeply interested in people and extremely patient, and more ascribed these traits to the G.P. than did the non-changers. In addition, more changers than non-changers saw the G.P. as sensitive to a wide range of factors when evaluating a medical problem. Since, as previously pointed out, fewer students who entered surgery and general practice changed their specialty choice, the present findings would indicate that students who are committed to these

two specialties perceive their fields differently than do students who have not made a firm specialty choice.

a) *Changers of Specialty Choice by Year in Medical School*

Pre-clinical and clinical students who changed their specialty choices differed significantly, particularly in their characterizations of the internist and psychiatrist. Significantly more pre-clinical students who changed their specialty choice saw the psychiatrist as interested in intellectual problems $p < 0.01$, interested in people $p < 0.05$ and sensitive to a wide range of factors when evaluating a medical problem $p < 0.01$ than clinical students who changed their specialties. More clinical students, on the other hand, saw the internist, rather than the psychiatrist, as possessing these traits and, more of them perceived the psychiatrist as a confused thinker $p < 0.01$.

b) *Non-Changers of Specialty Choice by Year in Medical School*

Regarding the traits ascribed to four specialties by pre-clinical and clinical students who did not change their specialty choices, significantly fewer clinical than pre-clinical students saw the surgeon and psychiatrist as interested in intellectual problems $p < 0.05$, however, more of the clinical students ascribed this trait to the internist. Neither group saw the G.P. as interested in intellectual problems. Significantly fewer clinical than pre-clinical students saw the surgeon, internist and G.P. as extremely patient, while more of the clinical students saw the psychiatrist as possessing this trait $p < 0.01$.

Changers of Specialty Choice by Type of Specialty Change

In order to examine whether students who changed specialties shifted toward technical-oriented or person-oriented specialties, the specialty groupings reported by Wasserman, *et al.*[2] were used. Technical-oriented specialties included general surgery, orthopedics, neurosurgery, urology, ophthalmology, obstetrics-gynecology, pathology, anesthesiology, radiology and ENT. Person-oriented specialties included internal medicine, pediatrics and psychiatry. While Wasserman, *et al.*[2] viewed general practice as a "mixed" specialty, our analyses indicated that general practice was more similar to the person-oriented specialties; hence, general practice was included with the other person-oriented specialties in the present paper.

Slightly more of the pre-clinical students who changed specialties shifted to technical-oriented specialties and clinical students who changed specialties tended to enter person-oriented specialties, however, this difference was not statistically significant. When pre-clinical and clinical students who changed specialties (N=203) were compared with students who did not change specialties (N=84), significantly more of the changers entered technical-oriented specialties, while more of the non-changers entered person-oriented ones ($X^2 = 5.71$; 1df; $p < 0.02$).

DISCUSSION

The study by Yufit and his colleagues[1,2] is the most comparable to the present study with respect to the time period during which changes in specialty choices were followed. In the present study 71 percent of the students changed specialty choices between the time they were students and entered practice, while Yufit found that only 43 percent of medical students changed specialties between their freshmen years and three years post graduation. However, it should be pointed out that Yufit studied only one class of students, while the present study included four classes. Nonetheless, even when the percentage of changers of specialty choice was considered for freshmen, sophomores, juniors and seniors separately (72 percent, 81 percent, 65 percent and 60 percent respectively), these figures are considerably higher than the 43 percent found by Yufit. Differences in the two studies may be due to differences between students in the two schools; and, in addition, factors such as religion, sex, marital status and parental social class, as well as clinical experience, have been found to influence specialty choice.[5]

Yufit also found that, in the clinical years, more students changed their choice from general practice to a specialty, while in the present study, significantly more students interested in general practice did not change

their initial career choice, despite clinical experience. However, interest in general practice apparently varies considerably among medical schools. Mount and Fish[5] found that interest in general practice ranged from 74 percent to 42 percent among students in several Canadian medical schools, and 55 percent of the students in these schools still maintained an interest in general practice as seniors. In the present study, significantly fewer students interested in general practice or in surgery changed their career choice. Clinical experience did apparently have an influence in changing career interests toward obstetrics-gynecology and radiology in both Yufit's and our studies, as significantly more students who changed specialties entered them.

Students who entered psychiatry did not show a significant career commitment to this specialty in medical school, as might be expected from the findings of other researchers.

The characterizations of surgery, internal medicine, psychiatry and general practice by students who entered the practice of these specialties were strikingly similar to the characterizations of these specialties by students who entered the practice of ENT, pediatrics, obstetrics-gynecology and radiology. Zimny[6] similarly found that the specialty choice of senior medical students did not significantly affect their characterizations of various medical specialists. He attributed this lack of difference to the common experience students have with various specialists during medical school. In the present study the characterizations of specialists did not differ greatly between students who changed and who did not change their specialty choices. The differences that did occur were primarily between how pre-clinical and clinical students characterized the internist and the psychiatrist. Clinical students saw the internist as more intellectual, more interested in people and having more breadth when evaluating a medical problem than the psychiatrist, while pre-clinical students saw the psychiatrist as possessing these traits more than the internist. In this regard, Yufit found that clinical experience tended to generate student interest in internal medicine.

Significantly more students in all four years in the present study who changed specialties entered technically-oriented specialties while more students who did not change specialties tended to enter person-oriented ones. This finding would seem to indicate that experience in medical school tends to reinforce students who are initially interested in person-oriented specialties, while medical school experience influences those who were undecided in their career choice to shift toward technically-oriented specialties. The introduction of clinical experience in the first year of medical school is unlikely to have much effect in influencing undecided students toward an early career choice, for the career alternatives in medicine remain numerous and the social welfare interests of many incoming medical students span several specialties. Recent social changes in universities and medical schools as well as the pressing problems in health services and health care delivery, are generating the need for more community-oriented physicians.[7] It would appear that this type of future physician is more likely to come from the ranks of those medical students who are initially person-oriented. All of these factors will doubtlessly alter past specialty images and sharpen differences in the educational demands and needs of person-oriented and technically-oriented students.

Data regarding the process of career choice in medical school are largely descriptive. This is due in a large part to the complexity of the process in which a majority of students playfully "try on" different roles during their medical school experience. Yet it appears that this process may change as students increasingly demand greater congruence between immediate and long-term educational goals, resist "institutionalization" and traditional professional role-models. Studies of the effects of the changing nature of medical education on the career choices of medical students would be enlightening.

SUMMARY

The present study compared attitudinal data regarding various medical specialties, obtained from 287 medical students, with their subsequent specialty choices upon entering medical practice. Seventy-one per-

cent of the students entered specialties which differed from their choices as medical students. More students who changed specialties entered obstetrics-gynecology and radiology, while more of the non-changers entered surgery and general practice. Differences in students' characterizations of surgery, internal medicine, psychiatry and general practice were related more to the degree of clinical experience in medical school than to differences between specialties entered. Changers and non-changers of specialty choice did not differ greatly in their characterization of the medical specialties considered, except clinical students saw the internist as more intellectual, more interested in people and having more breadth when evaluating a medical problem than the psychiatrist. Pre-clinical students tended to see the psychiatrist as possessing these traits to a greater extent than the internist. Significantly more of the students who changed specialties entered technically-oriented specialties, while more of the non-changers entered person-oriented ones. It seems likely that the community-oriented physician of the future will be drawn from the person-oriented pool of students. □

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Morse Kent Taylor—1823-1889 Pioneer Oklahoma Physician

EVERETT R. RHOADES, M.D.

Little has been written about many of the pioneer physicians in Oklahoma. Many of these early day physicians were unusual and a knowledge of their lives provides valuable information for the student of the history of medicine in Oklahoma. These physicians displayed a vigor and resourcefulness that would place them among the leaders of present day medicine in the state. Such a person was Morse Kent Taylor, Pioneer Oklahoma physician and surgeon U.S.A.

MORSE KENT TAYLOR was born in Watertown, New York on May 14th, 1823, but spent his early years in Michigan as a farmer's son.[1] As he grew to manhood he worked for a time as a cooper and contractor. During the Mexican War he entered the United States military service as a Lieutenant in the 1st Michigan Cavalry. He was mustered out July 10th, 1848. He entered medical school and graduated with honors in the second class of the University of Michigan in 1852. At the time he was approximately 29 years of age.

He practiced for a few years in Galesburg, Illinois, and in 1858-1859, was Chairman of Physiology and Hygiene at Lind Medical College (later to be the Chicago Medical School). This career was cut short by the outbreak of the War Between the States. Turning down a Colonelcy in the 4th Illinois Infantry (presumably as a line officer) he entered the Medical Service of the US Army as Surgeon of the 26th Illinois Infantry August 27, 1861. One year later he was appointed US Surgeon of Volunteers, a post he held until the close of the war. He was mustered out in October, 1865. His chair at Lind had been held for him but he apparently preferred practice in Keokuk, Iowa. He seemed to have developed a taste for military life however, because he accepted a commission as Captain and Assistant Surgeon, U.S.A. in May, 1867. He was 44 years of age.

He served in many areas but principally in Texas and the Indian Territory. He served in Texas from 1875 to 1879, chiefly in San Antonio, the place of his ultimate retirement. Following this he had tours in New York, Detroit, and at Fort Sill. It was at this latter duty station that his skills were demonstrated in many situations, but particularly in the field of sanitation.[2]

Medical conditions at Fort Sill at this time have been previously described[3] and can be described as exceedingly unhealthy. Most of the diseases were related to malaria, dysentery and typhoidal syndromes. All these conditions were directly related to the source and condition of water for drinking and bathing as well as other unsanitary conditions at the post.

The high incidence of disease caused editorial comment in the *Journal of the American Medical Society* of February 26th, 1887.[4] Doctor Taylor answered the editorial, vigorously defending the rapid improvement in conditions at Fort Sill between 1884 and 1887.[5] He gives a graphic account of some



Figure 1. Morse Kent Taylor, Major and Surgeon, Fort Sill.

of the conditions, especially malaria, affecting the men:

> When the writer entered upon his duties as Post Surgeon the latter part of November, 1883, the command, then consisting of four companies of infantry and two troops of cavalry, was in a most demoralized condition. Of the eleven officers for duty all had been sick during the two preceding months, three others were absent on sick leave, and of the enlisted men the rate of cases per 1000 mean strength was 468, exclusive of injuries, for the months of September and October, according to the records. These, however, did not express the real state of the case. As there was quite a rivalry in the target practice of the respective commands, the men would take their "shakes," then their quinine, and as soon as the fever abated, their turn at the rifle grounds, without going on the sick report.. From the representations of the company commanders it was evident that few men escaped.

He went on to describe a typical attack:

> Some of the attacks were of great severity. Men would be stricken down while on parades or at guard mount and have to be assisted to their quarters. One of the more common symptoms was intense pain in the back of the neck and base of the brain. Said an officer, referring to this symptom in his own case, that it struck him almost like an electric shock, and was the most excruciating suffering that he ever endured, or could imagine one capable of enduring and live.

Doctor Taylor was well aware of the reputation of the post at the time of his assignment and was determined to find the cause of so much illness and if possible correct the underlying conditions. He first carefully inspected the geology and natural surroundings of the post, as well as the duties and habitations of the men and he quickly eliminated these as important causes of malaria (thus, at least in part, rejecting the earlier "endemic" factors of Kilbourne).[6]

He next investigated the water supply which he found to be from two sources; a shallow well near the west line of barracks and a stagnant pool in the bed of Medicine Bluff Creek, northwest of the post. From the latter source water was obtained by driving a team and wagon into it, and dipping water into a tank. The water was then distributed into uncovered barrels in the vicinity of the barracks. He found the well water to be highly contaminated because of surface drainage from barracks as well as from the stables 250 feet away. The creek water in the barrels was even more offensive with a large amount of sediment. A distillate of this he noted to have a "faecal and urinous odor most nauseaus" not unlike that found in the water itself after 24 hours in a barrel during the summer. He stated that microscopic examination revealed too many organisms to be enumerated.*

Doctor Taylor found a spring at the northeast corner of the garrison which yielded a flow of eight gallons of water per minute. The surgeon in 1877 had condemned the spring because of the mistaken impression that it was fed by surface drainage. Doctor Taylor carefully analyzed the water and pro-

*This is the first clear notation of the use of a microscope at Fort Sill. It is likely one may have been in use sometime before 1884.

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Figure 2. Residence of Major Morse Kent Taylor.

nounced it one of the purest springs to be found in the country. He concluded its origin must be remote and unaffected by local rains or droughts. He convinced the commanding officer to assign a detail whose charge it was to enlarge the flow of water from the spring. By altering the outflow of the spring the flow was increased to more than 7,000 gallons an hour. These efforts led to an appropriation of $3,500.00 and a basin was excavated for storage and a stone spring house was erected. This building had four foot thick walls and was designed to protect the spring from floods and driftwood from the creek. An automatic valve was constructed to prevent water from the creek entering the spring during rises in the water level in the creek.

In 1885 the water was finally introduced into the buildings with a more closed system. The attack rate for malarial fevers, dysentery and diarrhea per 1000 mean strength shows a dramatic decline during Doctor Taylor's tenure:

Rate per 1000 M.S.

1883	1884	1885	1886
560	550	404	223

He pointed out that this was an illustration of the baneful influence of unpure water on the health of troops, since other conditions of their lives were little changed between 1869 and 1886.

The spring became a famous local landmark and was named "Ambrosia Spring" in honor of Doctor Taylor's wife. The couple had been married in Clinton, Michigan, April 25th, 1849. Mrs. Taylor died at Fort Sill in 1884 before completion of the work on the spring.

At Fort Sill Doctor Taylor entered actively into the social life of the post. He certainly must have been an interesting and gracious conversationalist. He is mentioned prominently and frequently in a delightful volume of letters by Marion T. Brown,[7] a young woman from Dallas who visited Fort Sill in 1886-1887. Doctor Taylor had an elaborate lap robe made of skunk skins (with the tails attached) which made a marked impression on the young girl.

On December 20th, 1886, a group gathered at Doctor Taylor's house to fill candy bags for the Christmas tree. At this time he was ill with a "cold" and chills for which he took as much as 20 grams of quinine. By January 25th, 1887 he was still quite ill and Miss Brown thought he was despondent over his impending retirement and the prospect of having nowhere or no one to go to. She felt he would "go to his last meeting place soon."[7]

One of Doctor Taylor's last official acts was to serve as a delegate from the Indian Territory to the annual meeting of the Amer-



Figure 3. Spring House, Fort Sill, Oklahoma.

ican Medical Association in St. Louis, May 4th-7th, 1886.[8] In 1886, Doctor Taylor also ordered a cleanup of the fort and established a dump for garbage which greatly improved sanitary conditions.[9]

In 1887, Doctor Taylor's service in the Army came to an end. Order No. 105 dated May 9th, 1887, noted the doctor's retirement on the following day:

> In the retirement of Doctor Taylor, the service loses an honorable and competent officer, and this garrison, a faithful and vigilant Post Surgeon, who was ever on the alert to protect his charge against the bad consequences of either their own careless habits, or the mistakes of the supply department. On such occasions, Doctor Taylor spoke in no uncertain terms as the records of the Adjutant's office show.
>
> Besides being a skillful physician, Doctor Taylor has attainments as a sanitary engineer; Fort Sill was fortunate in having the service of one so competent in designing and superintending the construction of a system of water supply.
>
> Since Doctor Taylor became the sanitarist of this post its standing in the order of health has greatly increased, and the post commander deems it proper on this occasion, in behalf of the garrison, to express their appreciation of his eminent services and to say that he will carry with him the kind wishes of all.

He retired to a home on Martin Street in San Antonio where he busied himself writing poetry, engaging in church, Masonic and business activities (the latter being with the rapid transit railway system) as well as conducting a practice.

The first notice of Doctor Taylor's final illness is in the San Antonio Daily Express of October 9th, 1889, which noted "Doctor Morse K. Taylor is confined to his room by sickness." On October 14th his condition had become critical and on October 19th, Doctor Johns, who was caring for Doctor Taylor noted his condition was "somewhat hopeful" compared to one day previously. He had been having chills until the day before. However, he was quite feeble and on Sunday, October 20th, 1889 at 5:30 in the afternoon, Doctor Taylor breathed his last. The only suggestion of the nature of his illness is that in the San Antonio Daily Express for Monday, October 21st, which noted that he suffered the formation of a prostatic abscess.[1] "He was unconscious for many hours at the end and uttered his last words the day before his death."

On October 22nd, 1889 he was buried in the National Cemetery at Fort Sam Houston. At the time of his death he was engaged in compiling a comprehensive study of the climatology of Texas. He left a son, Doctor F. M. Taylor, of San Antonio. More recent descendents have not been found.

Doctor Taylor made significant contributions to the medical literature. His lucid and forceful writing denotes a sound, scholarly observer. A tentative bibliography is listed in Table 1. □

Table 1
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921 N.E. 13th Street, Oklahoma City, Oklahoma 73104

ANNOUNCING
AMERICAN BOARD OF FAMILY PRACTICE
Certification Exams

The American Board of Family Practice will give its next examination for certification in various centers throughout the United States. The examination will be over a two-day period on April 29th, 30th, 1972. Information may be obtained by writing:

Nicholas J. Pisacano, M.D., Secretary
American Board of Family Practice, Inc.
University of Kentucky Medical Center
Annex #2, Room 229
Lexington, Kentucky 40506

DEADLINE FOR RECEIVING COMPLETED APPLICATIONS IS FEBRUARY 1st, 1972

Medicine in France

C. ALTON BROWN, M.D.*

Greediness for what people consider their fair share of medical care is ruining France.

THE RED TAPE and administrative muddles of France's method of socialized medicine are very painful and clearly point out many mistakes that we should avoid when the United States adopts a National Health Service.

In 1946 the French government created a single agency to administer welfare, health and hygiene programs throughout the country. (The last item being particularly important in a country where less than a quarter of the homes have running water and under 60 percent have indoor lavatories.)

In 1967 the social security code was extended to include the entire population.

An employee pays 35 percent of his salary to support the system; 6.5 percent directly from his paycheck; 17 percent from the employer for medical benefits, pensions and death benefits, and 11.5 percent from the employer for pre-natal allowances, maternity benefits, child allowances, payment to non-working mothers and rent assistance. Employers must also pay for the compulsory annual health check which state doctors carry out on all employees, but workers complain that a swift examination watched by perhaps 50 other people is both embarrassing and too cursory.

Medical treatment is not covered directly by the state, but patients are reimbursed for a high percentage of the cost involved. People are theoretically free to consult any doctor or specialist at any time, but the average citizen's anxiety to obtain the full health care to which he feels compulsory contributions entitle him, results in such heavy demands on doctors' services that many people are unable to see a doctor when they need him and must consult a "specialoid" instead. (Fees for specialists are higher than for G.P.s, and are reimbursed in the same proportion as G.P. charges.)

The majority of French practitioners agree to a fee schedule laid down by the state; patients are then repaid 80 percent of these fees. The patient gets considerably less if the practitioner has not agreed to the scale. Members of the profession complain that the fees are too low ($3 for an office visit; $5 for a house call), but if a doctor does not accept the fixed scale, he risks losing patients who want to collect maximum state reimbursement. Prescribed drug costs are reimbursed at between 70 percent and 90 percent depending on the type of illness involved.

Although repayment is supposed to arrive within a few days, the timelag usually extends to six to eight weeks.

*French Consul of Oklahoma City.

Only a minority of patients actually pay anything for treatment and drugs. In return for premiums, the insurance companies reimburse them the proportion of cost that the state does not cover. Thus the nation is encouraged to seek medical advice with great frequency and France is often referred to as "the most medicated country in Europe." A physician friend of mine in Allevard (Savoie) complained: "Greediness for what people consider their fair share of medical care is ruining this country."

In an official attempt to provide treatment for the really poor, of whom there are many, the French government runs "Dispensaries" at which patients are seen by state-employed doctors. Here there is no choice of doctor and very little in the way of consultation because it is possible to give only a minimum of time to each of the hundreds of people who attend. I visited one Dispensary. It was in a shabby back street and had decor reminiscent of a public lavatory. Dejected men and women shuffled in and sat on hard benches for two or three hours to get a couple of minutes medical attention.

Patients treated at public hospitals receive free treatment. Patients who use private hospitals are partially reimbursed in accordance with a fee scale.

Shortage of hospital staff is an increasingly desperate problem and the supply of general practitioners decreases yearly. France has an all-inclusive total of only 67,000 doctors for its 50 million citizens.

According to an article published recently in "Paris Match," the average net annual income of the doctors who agree to the government fee scale does not exceed $8,400. Income tax eats up one-third of a professional man's earnings.

Some French doctors have come to favor the idea of a salaried service because it frees them from the task of fee collection, but the majority are against becoming state employees. One French physician from the provinces said, "The question of money should not come between doctor and patient. Under present conditions I sometimes feel that the patient considers the receipt more important than his treatment." He goes on to say, "I didn't study for seven years to spend the major part of my day filling in certificates, making out receipts and explaining system procedure to my patients. Every consultation involves me in completion of at least four forms. Time spent in such trivia results in less attention to patients who really need medical attention. The method detracts from a good doctor-patient relationship and could be described better as an anti-social system rather than as a social one."

There is certainly little love lost between doctors and the government. Not long ago the profession complained that fees had risen only 15 percent in 20 years, and demanded an increase. The government at first turned down the request, but finally acceded under threat of strike . . . then retaliated by abolishing certain tax concessions previously enjoyed by the doctors.

A workman stood beside the Seine and said, "When the Security System began to take care of the nation's health it looked like good social progress, but over the years my countrymen have gone mad on medicines. French people abhor compulsion and in their anxiety to get full money's worth from what they must pay, rush to the doctor for drugs at every opportunity. They are poisoning themselves with pills and potions. French social medicine requires more than reform; it needs a revolution."

My own observations convinced me that the doctors of France will not stand for much more government interference and control. During the reign of socialized medicine the rules and regulations which govern their work (and even include instructions on how to run their private lives) have grown to 650 pages. Every doctor must possess and observe the articles of this weighty volume, but he does not receive it annually from the state which imposes its contents; to add insult to injury, he must purchase each current edition at a cost of eight dollars. □

1211 North Shartel, Oklahoma City, Oklahoma 73103

C. Alton Brown received his medical degree from the University of Oklahoma College of Medicine in 1942, where he is now Associate Professor of Clinical Medicine. His medical affiliations include the American Diabetes Association and the American Society of Internal Medicine. Doctor Brown is the French Consul of Oklahoma City.

News From The Oklahoma State Department of Health

TREATMENT OF NON-TYPHI SALMONELLOSIS

Although antibiotic therapy reduces the morbidity and mortality of typhoid fever and enteric bacteremias caused by other salmonella serotypes, antibiotics have not proven similarly effective for salmonella gastroenteritis. Despite this, antibiotics are often administered to patients with salmonellosis. Although indiscriminate use should be avoided, antibiotic therapy for salmonellosis would be justifiable if it shortened the duration of fecal excretion of salmonellae after illness, or improved the clinical status of the patient. In untreated salmonellosis, the period of postconvalescent fecal excretion lasts for a few weeks to many months, during which infected persons represent a potential source for the spread of infections to others. If antibiotics shortened this period of excretion, their use would provide a means of interrupting the transmission of the disease, especially in the confined school or hospital environment, and would thus be of value.

A number of superbly designed studies have now demonstrated that antibiotic therapy in acute salmonella gastroenteritis does not modify the clinical illness and *prolongs* rather than shortens the duration of post convalescent excretion. Early *in vitro* studies showing sensitivity of many strains of salmonella to a number of antibiotics (including chloramphenicol and ampicillin) have now been shown to correlate very poorly with *in vivo* antibiotic activity.

In addition to prolonging postconvalescent excretion, antibiotic therapy helps establish resistant strains of salmonella causing serious difficulties if subsequent systemic infection necessitates agressive antimicrobial therapy. Transfer of antibiotic resistance does occur among several species of enterobacteriaceae (including salmonella), constituting a definite health hazard.

Salmonella gastroenteritis is generally a mild, self-limited illness. Careful attention to fluid and electrolyte balance virtually assures complete and uneventful recovery.

New England Journal of Medicine,
Vol. 281, No. 12 □

COMMUNICABLE DISEASES IN OKLAHOMA FOR NOVEMBER, 1971

Disease	Nov. 1971	Nov. 1970	Oct. 1971	Total to Date 1971	Total to Date 1970
Amebiasis	2	—	4	53	52
Brucellosis	1	—	—	5	8
Chickenpox	6	60	7	204	2518
Encephalitis, infect.	4	1	8	41	17
Gonorrhea	710	635	1139	7556	6017
Hepatitis, infect. & serum	49	39	87	760	412
Leptospirosis	—	—	—	1	—
Malaria	1	11	2	68	103
Meningococcal infections	3	1	—	8	21
Meningitis, aseptic	2	4	9	117	43
Mumps	5	100	1	198	2395
Rabies in animals	3	4	16	270	88
Rheumatic fever	3	1	2	25	6
Rocky Mt. spotted fever	1	—	1	29	22
Rubella	1	8	5	70	822
Rubella, congenital syn.	—	—	—	—	—
Rubeola	1	211	2	794	791
Salmonellosis	13	11	22	182	151
Shigellosis	5	3	13	81	81
Syphilis	97	94	104	1150	1296
Tetanus	1	—	—	2	—
Tuberculosis, new active	24	36	24	306	309
Tularemia	—	—	1	17	8
Typhoid fever	—	—	1	3	1
Whooping cough	—	—	—	16	39

PHASE II AFFECTS PHYSICIANS

President Nixon's Price Commission has restricted increases in a physician's fees to 2.5 percent a year when justified by increases in costs, but granted the right of appeal to the Internal Revenue Service for a further increase for those physicians with greater increases in costs of conducting a practice.

New regulations also require that a physician maintain a schedule of fees and increases with a sign in his office that such a schedule is available for inspection. Unlike retail establishments, it is not necessary for the physician to post the fee schedule itself. He simply must have it available for inspection upon request.

The official regulations went into effect December 29th, one day before they were published in the Federal Register. The Commission earlier, December 15th, had announced guidelines on which the regulations were based. The guidelines took the form of a policy statement to be used by the IRS to enforce prior regulations as they applied to physicians and the new specific regulations.

While the new regulations and the guidelines were basically the same, the regulations did include a provision of an appeal mechanism for review of fee increases beyond the 2.5 percent limit. No exceptions were listed in the guidelines.

In summary the regulations state that a physician may increase his fees only to reflect his costs in effect on November 14th, 1971, and increases in costs after that date, reduced to reflect any productivity gains, and then only to the extent that the increased fees do not: (1) result in an increase in the physician's *profit margin;* and (2) do not result in aggregate fee increases in excess of 2.5 percent a year. *Increases above this percentage require prior approval by IRS.*

If a physician does increase his fees and this results in a higher profit margin, he could be subject to a $2,500 civic penalty or a $5,000 criminal penalty. However, if he does not increase his fees and his profit margin increases due to either increased productivity or economies in his practice, the penalties cannot be applied.

If a physician does find it necessary to increase his fees beyond the 2.5 aggregate, he can apply to the IRS for permission. His request must be submitted in writing to the District Director of Internal Revenue Service and must state the reason why the exception is being requested and contain sufficient information to establish that two criteria have been met: That the application of this new law would result in a serious hardship or gross inequity and that the request for an exception does not have "as one of its principle purposes the avoidance of the purpose of the economic stabilization act of 1970, as amended. . . ."

The section of the policy statement guidelines dealing with the maintaining of a fee schedule is not clear. While it is not necessary for the physician to actually "post" his fee schedule, he must make it available upon request. An IRS publication interpreting the regulations for the general public states, "Each retailer must display prominently at the place of sale the base prices of . . . the 40 items in each department which have the highest dollar sales volume, or the items which account for 50 percent of the dollar volume of sales in that department, if these are fewer than 40 items." Such lists were to be displayed by the affected retailers starting January 1st.

Until clarifying regulations are issued, the above cited requirement would appear to apply to physicians. This would mean that a physician could keep available a fee schedule on his 40 most common procedures, *i.e.,* office calls, hospital visits, lab tests, etc. If he finds that 50 percent of the entire dollar volume of sales in his practice is from fewer than 40 items, then these could be listed. The schedule must show the fee he was using during the price freeze starting on August 15th, and his current fee, if there has been a fee increase.

The text of the Price Commission's policy statement said, "A sign shall be posted in a prominent place in each facility stating the availability and location of the (fee) schedule." No suggested wording for the sign was given. □

Physicians Not Claiming Nursing Home Visits

Oklahoma's Department of Institutions, Social and Rehabilitative Services has presented figures to the Bureau of Health Insurance documenting the fact that physicians are making nursing home visits and not billing for them.

Formerly known as the Department of Public Welfare, DISRS is required to review nursing home records to assure that quality control programs are being implemented. In conducting the reviews the department documented 7,002 visits on 855 patients in nursing homes by 234 physicians. Five thousand nineteen of these visits were not billed for, 71.68 percent of the known visits.

L. E. Rader, Director of DISRS stated, ". . . we have documented information which the department has always believed to be true, that is, that physicians render many more services than those for which they bill." He went on to state that the figures had been presented to a regional meeting of the Bureau of Health Insurance, Division of Quality Control.

In a letter to Mark R. Johnson, M.D.. Editor of the *OSMA Journal,* Rader stated, "We feel that (this) is worthy of note and is a record of which physicians can take some pride." □

Amphetamine Quotas Set By Justice Department

Using authority granted to it by the 1970 Drug Abuse Prevention and Control Act, the Justice Department has proposed production quotas to cut by 40 percent the amount of amphetamine and methamphetamine manufactured by U. S. drug companies in 1972.

Attorney General John N. Mitchell said the Bureau of Narcotics and Dangerous Drugs (BNDD) proposed to limit national production of amphetamines to 5,870 kilograms and methamphetamine to 2,782 kilograms—an approximate 40 percent cut from 1971 production and a 70 percent cut from what was requested by drug companies.

Mitchell said 9.356 kilograms of amphetamine and 4,926 kilograms of methamphetamine were produced in 1971. The drugs are used to treat narcolepsy, a form of sleeping sickness, and hyperkinesis, a form of hyperactivity found in children. They also have been used widely for weight control, although such use is questionable.

In September of last year, Lucien M. Pascucci, M.D., President of the OSMA, called on all Oklahoma physicians to voluntarily limit their prescriptions for amphetamines and methamphetamines. This plea was made in response to a call from President Nixon for the medical profession to take the lead in stemming the problem of drug abuse.

Prescription limiting was endorsed by medical associations throughout the country and has lent support to the BNDD's call for limiting production of amphetamines.

BNDD has estimated that large amounts of the legally produced drugs have been diverted into illicit drug traffic. Even though only a small amount of this comes through physician prescriptions, the production quotas will limit the amount that can be stolen or misdirected.

The 40 percent production cut was recommended by the Department of Health Education and Welfare. The proposed quota is the first time the government has used this authority under the 1970 Drug Abuse Prevention and Control Act.

Legal use of amphetamines could be curtailed as a result of a current Food and Drug Administration Evaluation Study of their effectiveness as a weight reducing drug. The study will take two to six months, but the FDA already has ordered the amphetamine manufacturers to submit additional proof of effectiveness because of critical conclusions by the National Academy of Sciences. □

Osteopaths Push For Tulsa School

Establishment of a College of Osteopathic Medicine and Surgery in the Tulsa area has been called "feasible" by a report prepared for the Oklahoma Legislative Council. The report is one of two that will be considered by the Legislature in its upcoming session. One dealing with an osteopathic school, and the other with a medical school.

A former director of the Office of Education of the American Osteopathic Association, Lawrence W. Mills, prepared the Osteopathic School Report. In his closing summary he states, "A college of Osteopathic Medicine and Surgery in Tulsa is feasible. This report indicates that such a college would contribute materially to the solution of existing health problems facing Oklahoma." He went on to say, "A State College of Osteopathic Medicine in Tulsa would produce a constantly increasing number of general practitioners in the less populated areas of the state."

Mills placed great weight on the fact that over 75 percent of the D.O.s are in general practice. ". . . members of the last ten graduating classes of colleges of osteopathic medicine, who have started practice in Oklahoma, illustrate how the osteopathic profession is *contributing most of the GPs to the non-metropolitan areas of the state,*" he said.

While implying that much of the construction cost of a medical school is oriented to specialty training, the report said, "The construction cost of a college of osteopathic medicine and its cost of operation would be considerably less than those of a professional school which is oriented to highly specialized and research training . . . the osteopathic profession and its colleges acknowledge the importance of research and the specialty training—but not at the expense and training of general practitioners."

Estimated cost of constructing a 140,000 square foot osteopathic school in Tulsa was $13,000,000, excluding the cost of land and architectural fees. Yearly operating budget for the school is estimated at $2,825,000 based on appropriations and student tuition.

The entire report promotes the feasibility of an osteopathic college with a planned admission of 64 students per year, for a total of 250 students after the start of the fourth year of operation. It stressed that a federal construction grant of approximately $8,700,000 might be available under recent legislation, with a $4,300,000 state matching fund.

A report regarding the feasibility of a medical school in the Tulsa area is under preparation. □

Midwest Cancer Conference To Convene

The Kansas Division of the American Cancer Society will present the 24th Annual Midwest Cancer Conference on March 17th-18th, 1972 in Wichita, Kansas. Theme for the two-day conference will be "Cancer Progress in the 70's."

Nine prominent guest lecturers will appear on the program. They are: Denis P. Burkitt, M.D., Uganda, Africa and London; Elizabeth Kubler Ross, M.D., Chicago; Melvin Tefft, M.D., Boston; Tague C. Chisholm, M.D., Minneapolis, Minnesota; Sharad D. Deodhar, M.D., Cleveland, Ohio; Richard Alan Oberfield, M.D., Boston; John S. Stehlin, M.D., Houston, Texas; Donald A. Shumrick, M.D., Cincinnati; and William R. Roy, M.D., Topeka, Kansas.

All physicians in the midwest are urged to attend the graduate course on cancer. □



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AMA Actions in Brief

The AMA has issued a brief synopsis of the actions taken by its House of Delegates during the Clinical Convention in New Orleans, November 28th-December 1st. The following is a brief explanation of some of the more important actions.

● In regard to contracts between physicians containing a restrictive covenant, the House of Delegates reaffirmed the action of the Judicial Council and stated, "There is no ethical proscription against suggesting or entering into a reasonable agreement not to practice within a certain area for a certain time, if it is knowingly made and understood. Whether it is advisable as being in the best interest of the public is debatable. Perhaps such an agreement should not become operative until after one year or should expire after it has been in effect for a period of five or so years.

"Ethically such agreements are not forbidden, but they should be entered into with caution."

● In regard to peer review committees operated by medical societies the AMA House resolved, "That the American Medical Association urge all health insurance carriers and governmental health financing agencies to rely on appropriate medical peer review programs for adjudication and resolution of all matters concerning the quality, cost or utilization of medical services which require professional judgement;" and that "it is the responsibility of state medical associations, county medical societies and hospital medical staffs to create active and effective systems of peer review which are responsive to the needs of their respective communities;" and closed by stating, "that peer review programs shall have as their goal both improved quality of medical care and more efficient delivery of medical services."

● Resolution 15 was introduced by the Oklahoma delegation and dealt with the inequities of Medicare reimbursement between physicians in practice in rural communities and those in urban areas. The resolution as adopted stated, "Since the cost of medical practice is now substantially the same in many rural and urban areas, any inequality in reimbursement for services of rural physicians based on arbitrary differentials between these two areas should be eliminated."

● Resolution 16 calling for insurance against mental illness was also introduced by the Oklahoma delegation. A substitute resolution was adopted stating, "That the AMA encourages support of health insurance programs which would include payment for the cost of treatment of surgical and medical ills, including psychiatric disorders when requested."

● A substitute resolution was adopted urging governmental agencies to avoid the use of the terms "provider" and "consumer" when the terms "physician" and "patient" were more appropriate.

● Direct billing of patients by physicians was called for in a resolution to recommend to the Congress of the United States and the Department of HEW that any future federal programs which pay for care by private physicians permit direct billing and that such provisions allow payment to the patient when the physician and patient concur.

● Resolution 14 regarding medical school admission policies was also introduced by Oklahoma. Even though amended, it was adopted substantially as written. It was resolved "that the Council on Medical Education of the AMA recommend strongly to all medcal schools that their admissions committees include a significant proportion of practicing physicians . . . (and) that the Council . . . evaluate available motivational tests which would add another objective yardstick for measuring an applicants overall fitness to become a medical doctor and to formulate recommendations thereby . . . (and finally) that the Council work in cooperation with the association of American Medical Colleges toward implementing the foregoing recommendations . . ."

● A resolution opposing National licensure of physicians and supporting State Boards of Examiners and Interstate Reciprocity of state licensing was adopted by the House of Delegates.

● Physician visits to extended care facilities came under consideration when the House affirmed that, "In the interest of the best patient care, the frequency with which patients are seen is properly the decision and responsibility of the physician, subject to proper and recognized review by his peers; . . ."

● The House approved a plan by the AMA Board of Trustees to study the feasibility of publishing a monthly socio-economic journal. It is anticipated that the journal will be self-sustaining and that it will incorporate material from other AMA publications currently produced at considerable expense.

● Two resolutions calling for tax incentives for physicians to practice in rural and urban areas were referred to the AMA's Board of Trustees and its Council on Health Manpower for consideration. Instructions were that the two resolutions would be reconsidered at the 1972 annual convention in San Francisco.

● The retiring Executive Director and Founder of the American Academy of General Practice, Mr. Mac F. Cahal, was chosen by the AMA House of Delegates to receive the citation for Distinguished Service by a Layman. The citation will be presented in San Francisco. □

Legislature Doctor Busy But Appreciated

Numerous numbers of both the Oklahoma Senate and House of Representatives have expressed their appreciation for the OSMA volunteer "Doctor of the Day" program. During each legislative session the medical association equips and stocks a first aid station on the fourth floor of the Capitol Building to serve all members of both houses.

The physicians manning the First Aid Station during the opening days of the Legislative Session found it to be a busy place. Each one volunteered to come to the Capitol Building and serve one full day.

Known as "Doctor of the Day," each volunteer is introduced at the opening session of both houses and

is allowed on the floor of the House and Senate while they are in session. This is a privilege afforded to few persons.

Physicians interested in serving during the months of February and March are asked to contact Dave Bickham, Associate Executive Director of the OSMA, for further information. Since the doctor serves only while the two houses are in session, this limits service days to Monday through Thursday of each week. The Legislature adjourns at noon on Thursday.

The 1972 Legislative Session marks the seventh year that the OSMA has sponsored the volunteer program, which has become a model for others throughout the country.

A "Nurse of the Day" is in the station each day and is a volunteer sponsored by the Oklahoma State Nurses Association. □

Three Oklahomans Receive AMA Appointments

Three Oklahoma physicians are listed among those appointed to serve on AMA Councils and Committees. Doctors Rex Kenyon, Kieffer Davis and Dale Groom, were each reappointed to new one-year terms by the AMA's Board of Trustees at its December meeting.

Members of the AMA Councils and Committees serve one-year terms, with a maximum tenure of ten consecutive terms. It is necessary for them to be reappointed each year.

Rex E. Kenyon, M.D., Oklahoma City pathologist, was reappointed to the AMA's Council on Legislation. He can be reappointed to this Council until 1979. Doctor Kenyon, a past-president of the OSMA, has been active in both the Oklahoma and American Medical Political Action Committees.

Doctor Kieffer Davis, an occupational medicine specialist from Bartlesville, was reappointed to the Council on Occupational Health. He has already served a number of years on the Council and can be reappointed until 1974. He served a number of years on the OSMA Occupational Health Committee.

The Director of Oklahoma's Regional Medical Program, Dale Groom, M.D., Oklahoma City, was reappointed to the AMA's Council on Scientific Assembly. This is the Council that supervises the scientific portion of the biannual AMA meetings. He can be reappointed until 1974. □

Investigating Committee Issues Report

Five recommendations to improve nursing home care have been made by a special nursing home investigating committee of the Community Relations Commission. During a period of approximately seven months the committee personally visited 26 nursing homes, at least three times each, and observed the operations and activities in each.

During each visit the nursing home was asked to fill out a short questionnaire and then, at the conclusion of the visit, each committee member transferred their observations to a report form. At a meeting to write the final report, the committee carefully weighed each of the written observations as to merit and to importance both to the residents and nursing home employees, including administrators.

The committee observed that nurses' aides lacked ". . . proper geriatric training to adequately perform their duties in caring for the multiple and various needs of the residents." They recommended the creating of a special training program and issued an appeal to the State Department of Vocational and Technical Education and the Nursing Association to foster the program.

The report stated, "We find understaffing of professional personnel," and went on to recommend, "more supervision in this area by proper authorities, thus forcing conformity to state requirements by all."

The committee recommended that menus provided to nursing homes by hired dietitians be followed more closely with less substitution of other foods than listed on the posted menu. They also called for more closely supervised serving of food to residents unable to feed themselves."

The committee's fourth observation and recommendation was somewhat cryptic and stated, "We find discrepancy in the charges for services and supplies furnished by the homes." They then recommended, "that a standard charge be mendatory for all homes. This does not apply to welfare payments or items covered by Medicare. This applies to charges made by nursing homes for extra services and supplies required to care for the residents."

The last recommendation was in regard to attitude and atmosphere in nursing homes and called for "empathy and open lines of communication."

The final report of the committee was transmitted to the Community Relations Commission for information and implementation. □

NOTICE

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Physicians wishing to bring claims to the committee should address them to OSMA Medical Insurance Review Committee, 601 N.W. Expressway, Oklahoma City, Oklahoma 73118. □

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New Name For Medical School

The name of the University of Oklahoma Medical Center has been changed to the University of Oklahoma Health Sciences Center, Leonard P. Eliel, M.D., OU Executive Vice-President for center affairs, announced recently.

Doctor Eliel said he had been notified that the State Regents for Higher Education have approved giving the center the new name which more accurately reflects the multiple educational programs, service and research functions which have developed on the Oklahoma City health campus in recent years.

"The name 'medical center' is misleading and confusing since it suggests to many that the medical school is the only academic function and that medical education is our only program," he explained.

The present health sciences complex includes schools of medicine, nursing, health, dentistry and allied health professions, a graduate program in the medical sciences, the two University of Oklahoma Hospitals, the OU Speech and Hearing Center and the University Family Medicine Clinic.

When the health campus was officially designated the University of Oklahoma Medical Center in 1956, the only major academic units were the Schools of Medicine and Nursing.

The State Regents for Higher Education also authorized re-naming the Health Sciences Center schools "colleges" in conformity with the nomenclature used on the Norman campus.

Here are the new names:

College of Medicine, College of Nursing, College of Dentistry, College of Health and College of Allied Health Professions. The sixth academic unit has always been called the Graduate College-Medical Center.

Proposals of the center administration to re-name the center and the schools were approved by the OU Board of Regents in November and then submitted to the State Regents for final action. □

OHA To Present Guest Lecturer

W. Proctor Harvey, M.D., Professor and Chairman of the Division of Cardiology, Georgetown University, Washington, D.C., will be the Visiting Professor for the Oklahoma Heart Association in February.

Doctor Harvey will conduct sessions at St. Anthony Hospital, Oklahoma City, beginning at 8:00 a.m., February 8th, 1972. That afternoon, he will be at Baptist Memorial Hospital in Oklahoma City.

Tuesday evening, following a dinner at the Faculty House, 500 N.E. 14th Street, Oklahoma City, Doctor Harvey will give a presentation.

February 9th, Doctor Harvey will speak during Grand Rounds at the University of Oklahoma Health Sciences Center at 8:30 a.m. and will spend the remainder of the day at the medical center.

On Thursday, February 10th, he will attend Grand Rounds at the Tulsa Medical Education Foundation at the Red Cross Building, 35th and South Harvard, from 8:00 to 9:00 a.m. From 9:30 until 12:00 noon, Doctor Harvey will make Grand Rounds at St. John's Hospital.

All physicians are urged to hear this outstanding teacher and clinician. □

DEATHS

JAMES R. REED, M.D.
1900-1971

James R. Reed, M.D., Chairman Emeritus of the University of Oklahoma College of Medicine, Department of Ophthalmology, died in Oklahoma City, December 29th, 1971. A native of Nebraska, Doctor Reed came to Oklahoma as a child and graduated from the OU Medical School in 1927. He practiced his specialty, ophthalmology, in Oklahoma City until his death.

Doctor Reed's medical affiliations included the Oklahoma City Academy of Medicine and the Oklahoma Eye, Ear, Nose & Throat Academy.

ROBERT H. JOHNSON, M.D.
1913-1971

Robert H. Johnson, M.D., retired orthopedic surgeon, died in Tulsa, November 25th, 1971. A native of Elk, Washington, Doctor Johnson graduated from the Washington University School of Medicine in 1940.

Doctor Johnson served with the Air Force during World War II. He had practiced in Tulsa since 1948, retiring last year.

G. Y. McKINNEY, M.D.
1886-1971

A pioneer, Henryetta physician died November 30th, 1971 in Okmulgee. Doctor McKinney, who was born in Mena, Arkansas, graduated from the University of Arkansas Medical School in 1912. He began his practice in Emmet, Oklahoma. In 1917 he moved to Henryetta where he remained until his retirement in 1966.

Recognizing his service to humanity, the OSMA awarded Doctor McKinney a Fifty Year Pin and in 1962, they again honored him with the presentation of an Honorary-Life Membership.

ROXIE A. WEBER, M.D.
1894-1971

A former Assistant Director and Director of the Oklahoma State University Medical Service for 22 years, Roxie A. Weber, M.D., died November 30th, 1971. A native of Ellington, Texas, Doctor Weber graduated from Johns Hopkins University School of Medicine in 1921. For five years she was a Laboratory Director at Sinai Hospital in Baltimore. Following further training in Europe, Doctor Weber came to Stillwater in 1942 to work in the university medical service. □

Health Careers Council Active

The shortage of health manpower is no new phenomenon to America in the 1970's: Lack of sufficient numbers of all types of health workers has plagued the nation for decades. As medical knowledge has increased and the delivery of health care has become more sophisticated, the quantity of skilled personnel has failed to meet the demands by increasing margins.

In order to coordinate operations to alleviate the health manpower void in Oklahoma, OSMA and other leaders in the health field, established the Oklahoma Council for Health Careers in 1967 with the primary purpose of recruiting for all health professions. Funds to operate the Council were to come from membership dues paid by hospitals and health organizations. At the present, membership in the Council has grown to include 22 organizations, 25 hospital auxiliaries, and 60 hospitals.

In the four years which have lapsed since the formulation of the Council, many activities have been undertaken. These can be grouped under major headings of informing, motivating, counseling, and recently placement of health trained, ex-military personnel. Present staff members of the Council include Kenneth Hager, executive director; Floyd Nicholson, coordinator of Operation MEDIHC; Paige Pfeifer, coordinator-school activities; James McCarver, education counselor; Doris Deaton, secretary; and Judy Davis, secretary.

The non-profit organization has acted as a central clearing house for health career information, providing data, pamphlets and films on over two hundred health professions. In order to increase requests for health career information, the Council has mailed colorful, eye-catching placard kits to all state schools, libraries, and hospitals, inviting interested persons to write the Council for information. Requests for health career information have risen until over 1,000 inquiries are received monthly.

A special, computerized system is used to note location and vocational interest of individuals requesting this information. Colleges and vo-tech schools are given addresses of individuals ripe for recruiting into their health training programs.

While the information section forms a base for Council activities, assembly presentations are given to state high schools and colleges in an effort to stimulate interest in health careers. A touring, hour-long program was presented to 65,000 students last year in 165 individual performances. The program features a professional musician who gains the attention of young audiences and then follows up with a thirty-minute, multiple slide projector presentation on health careers.

The Oklahoma Council for Health Careers also charters and assists Oklahoma Health Science Clubs, an organization of high school clubs whose members are interested in various health professions. The clubs are mostly from large school systems that can support sufficient numbers of interested students. Twenty-seven clubs are now participating in the organization, and total student membership is 950 and growing. Many clubs were started by the efforts of physicians and physicians' wives. The Oklahoma Health Science Club generates a newsletter, *The Internal Inquirer*, and holds an annual convention at one of the state college campuses. This year the convention will be held at East Central State College at Ada.

While the Council serves to give career information to individuals, it is also involved in informing counselors in all Oklahoma institutions. Special workshops are held for

Oklahoma Medical Assistants Place Third



Oklahoma Medical Assistants placed third in the numerical increase category for new membership at the recent annual convention of the American Association of Medical Assistants in Atlanta.

Shown receiving the award is Virginia Waddle who works under the supervision of Curtis Cunningham, M.D., at the Methodist Home in Clinton. □

counselors in the Oklahoma City and Tulsa areas annually. A directory is published and distributed to state counselors, providing comprehensive information on health education in Oklahoma.

The Oklahoma Council for Health Careers also coordinates Operation MEDIHC (Military Experience Directed Into Health Careers). The MEDIHC program is coordinated on a national level by the Department of Defense and HEW. Since May 1970, the MEDIHC program has provided placement and job counseling services to over 280 applicants. Many of the individuals desire to continue training and the MEDIHC counselor has provided information on various health training facilities available.

During its four years of development, the Oklahoma Council for Health Careers has slowly moved toward becoming a total health manpower system, offering not only recruiting and motivation services, but counseling and placement services as well.

Future activities require much research and planning, a stage which the Council is presently in. Much additional information is necessary to determine the population needs, present health manpower needs, and future health manpower trends.

Of particular emphasis in the Council's planning is providing more skilled health manpower to Oklahoma's underserved areas, especially rural sections.

Although the problem has failed to develop to date, the Council feels particularly responsible to avoid over-recruiting and the personal tragedies resulting from over supply for the existing job market.

Such goals demand involved research and planning, plus the cooperation of all facets of the health industry. Since the Oklahoma Council for Health Careers is governed by a board of health professionals representing major health associations and organizations, it is in a key position to work toward such goals. □

Forum on Government Set By Auxiliary

"Know your state government" is the theme of a forum on medicine and government planned for the State Capitol Building Wednesday, January 26th. The program is sponsored by the Woman's Auxiliary to the OSMA and hosted by the Oklahoma County Auxiliary.

The first hour of the program will be devoted to an explanation of the three branches of government. The Honorable David Hall, Governor of the State of Oklahoma, will explain the Executive Branch. Marian P. Opala, Administrative Director of the Oklahoma Court System, will discuss the Judicial Branch, while the various aspects of the Judicial Branch will be discussed by Senator Finis Smith, President Pro-tempore of the Oklahoma State Senate, Representative Rex Privett, Speaker of the House of Representatives, and by the two minority leaders, Senator Denzil Garrison and Representative Charles Ford.

A special one-hour session on "People In Action—How to Influence the Legislative Process" is scheduled just prior to the lunch hour. R. Barton Carl, M.D., Chairman of the OSMA Legislative Committee will serve as moderator.

The legislators viewpoint will be presented by Senator Richard Stansberry, M.D., and Representative C. H. Spearman, Jr. David Bickham, Associate Executive Director of the OSMA and its registered lobbyist will give the "Lobbyists Viewpoint."

The importance of medical political action, such as AMPAC and OMPAC, will be explained by Rex Kenyon, M.D., a member of the AMA's Legislative Council and Past-President of the OSMA and Past-Chairman of OMPAC.

The afternoon will be devoted to visits to the House of Representatives and the State Senate.

The meeting will start at 9:00 a.m. with a reception and registration in the Blue Room of the State Capitol Building. Auxiliary members are urged to invite their State Senator or Representative to attend the reception. The formal program will begin at 9:45 a.m. □

Medical Examiners Name P.A. Advisory Committee

Three Oklahoma physicians and a physician's assistant have been named by the State Board of Medical Examiners to its Advisory Committee on Physician's Assistants. Meeting on December 4th, the Examiners appointed the committee in order to activate its rules on P.A.s which had been previously adopted.

The three physician members of the committee are Roger J. Reid, M.D., Ardmore; Francis R. First, M.D., Checotah; and Arthur W. Horsley, M.D., Oklahoma City. The P.A. named to the committee is William D. Stanhope of Oklahoma City.

According to the action taken by the examiners the committee is empowered to choose other advisors whose expertise may be helpful to it.

The committee's mission is to advise the board on requirements for postgraduate education, continuing education, evaluation / re-evaluation and/or certification/re-certification of the competence of a P.A. and on standards of educational programs for their training.

In the letter to the newly named committee the board specifically requested help on these points: definition of physician's assistants, preparation of a less informal and more standardized application procedure, manner of information regarding P.A.s' applications to the physicians in the state, and any legislative needs that they might foresee.

One of the rules adopted by the examiners required that its advisory committee should be composed of a representative of the faculty of a physician's assistant education program, a physician's assistant graduate of an accepted program at a baccalaureate level, and at least two members of the Board of Medical Examiners and any other individuals whose expertise the Board might find helpful. □

Tulsa Health Department Reports VD Awareness Month

November was Venereal Disease Awareness Month throughout Oklahoma and several county medical societies and city-county health departments conducted extensive information programs. The Tulsa City-County Health Department has released a report of its activities during November.

The total number of VD clinic visits at the Tulsa City-County Health Department during November was 520, as compared to 430 for the month of October and 290 for the month of September. The similarity between the October and November figures could be explained by the advanced publicity given Venereal Disease Awareness Month during October.

In the age group of 13 through 19 years there were 112 visits in September, 125 visits in October, and a jump to 209 visits during November. Visits from 20 year olds nearly doubled from 36 in October to 70 in November.

Visits in all categories were up during November, except for the 21 through 29 year group. For some unknown reason the increase visits came during October, from 104 visits during September to 234 during October and dropped back to 141 during November.

During the first 11 months of 1971 Tulsa County reported 1,528 cases of gonorrhea, an incidence of one case per 265 persons in Tulsa.

In the report, Betty Conrad, M.D., Chief of the Medical Care Division stated, "An appalling proportion of our citizens, of all ages, are grossly uninformed or even misinformed about venereal disease. The beginning of the breakdown of the hush-hush about venereal disease in the 1930s apparently gave us a present generation of parents of teenagers themselves poorly informed. Having become a wife and mother or a husband and father does not automatically make one an authority on venereal disease."

In another part of the report Doctor Conrad stated that spread of information has resulted in diagnosis and treatment of increased numbers of VD cases. □

Doctor Dixon To Present OMRF Lecture

Frank J. Dixon, M.D., Chairman of the Departments of Biomedical Research and Experimental Pathology at Scripps Clinic and Research Foundation, La Jolla, California, will present the second in a series of four Oklahoma Medical Research Foundation Lectures.

The Lecture, entitled "The Pathogenesis of Chronic Glomerulonephritis," will be given at 4 p.m., February 1st, 1972 in the East and West Lecture Halls of the Basic Science Building, University of Oklahoma Medical Center, Oklahoma City.

The Oklahoma Medical Research Foundation Lecture Series was established July, 1971, by the Foundation's Board of Directors as a means of providing a valuable service to practicing physicians throughout the state as well as the staff of the OU Medical Center.

The third OMRF Lecture will be delivered March 14th by Doctor Sol Sherry, Chairman of the Department of Internal Medicine and Physician-In-Chief, Temple University School of Medicine and Hospital, Philadelphia, Pennsylvania. His subject will be "Thrombosis." □

Sisters Endow Rural Medical Scholarship

Two sisters have privately endowed a rural medical scholarship for the University of Oklahoma's School of Medicine. To memorialize M. C. "Billy" Shibley, a Tulsa army pilot, the scholarship was created by Miss Jewel O. Leeright and Mrs. Leora Williams.

The two women set up $7,000 endowment fund which came originally from the estate of their aunt, the late Mrs. Mayme (Shibley) Swanson, Billy's mother. Recipients of the scholarship will be known as "Billy Shibley Scholars" and will be medical students interested in serving in rural areas of Oklahoma.

Doctor Leonard P. Eliel, Executive Vice-President of the OU Medical Center, expressed appreciation for the gift and noted that its establishment was consistent with the efforts of the university and state legislature to encourage medical school graduates to go into rural practice in Oklahoma by providing scholarship and loan funds for that purpose.

Billy Shibley, an OU law graduate who also studied three years at Tulsa University, was killed in November, 1941, at the age of 25 when his Army-Air Force observation plane crashed.

Arrangements for administration of the fund were made by Lee O. Teague, Medical Center Development Officer, and David Bickham, Associate Executive Director of the OSMA. Scholarship selections will be made by a committee of the association and the medical center. □

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Book Reviews

CURRENTS IN AMERICAN MEDICINE: A Developmental View of Medical Care and Education. By Julius B. Richmond, M.D., Dean, The College of Medicine, State University of New York. 133 pp. Cambridge: Harvard University Press. 1969. $5.50.

Of the several books which have appeared recently dealing with various aspects of the system of American medicine, this is indeed one of the best. The author, at the time of writing, Professor of Pediatrics and Head of the Department and Dean of the College of Medicine, State University of New York, Syracuse, is well qualified because of his experience and interests in these areas. In addition to his medical education background, he was the first Director of the Office of Economic Opportunity and initiated the Head Start Program. Thus, he is well acquainted not only with various facets of medical education and health care, but also with the relationship of the Federal Government to this field.

This small book gives an overview of the changes which have been taking place in the field of health over the past several decades. It is divided into five sections. The first, entitled "Educational Revolution and the Guild Establishment," covers the period 1900-1940. Beginning with the impact of the Flexner period on medical education in the first decade of this century and the rise of organized medicine as the force determining the medical care system of the country, Doctor Richmond presents a critical analysis of the resulting establishment, stressing that little attention was given to the reorganization of health services. The second section, entitled "The Scientific Revolution and the Academic Establishment," which covers the period 1940-1960, relates the dramatic advances in biological research and the enormous growth in federally funded medical research. In the next section, entitled "The Consumer Revolution: Translating Knowledge into Programs," covering the period 1960-68, he points out the growing tendency for the citizens of the country to desire more direct benefits resulting from new knowledge, and the need for expansion of the health services through legislation. Doctor Richmond points out that the first group practice prepayment health service plan was organized in Oklahoma.

In the final two sections, Richmond reviews some of the conceptual issues and problems facing the medical profession. He discusses the fragmentation of health services, efforts to deal with such problems through new legislation and the development of a national health program. He discusses also the roles and relationships of the hospital, the university medical center, the community health center and various group prepayment plans.

Richmond does not avoid controversial issues. While emphasizing the conservatism of the American Medical Association, he also pointedly documents the lack of leadership displayed by the Association of American Medical Colleges and by the schools of medicine. His fair treatment of these issues is clearly evident throughout.

This small monograph is packed with valuable information and is quite readable. It is to be strongly recommended.—*Harris D. Riley, Jr., M.D.*

PEDIATRIC UROLOGY. Edited by D. Innes Williams, M.D. 569 pp. New York: Appleton-Century-Crofts, 1968.

This is an excellent book. It is written in the main by four pediatric urologists from England so that the emphasis is predominantly but not wholly surgical. Medical aspects are covered by other British authors and there is a chapter on radiologic investigation by Chrispin of the Hospital for Sick Children, Great Ormond Street, London.

The traditional dogmatism so frequently seen in textbooks by surgical specialists is noticeably absent. The surgical contributions reflect, in a refreshing way, the experience of the authors who state their personal views rather than merely reiterating prevailing opinions. The medical sections are not as strong. For example, the quotation of an 80 percent plus recovery rate in acute glomerulonephritis is certainly conservative. This may be due to failure to differentiate poststreptococcal and nonstreptococcal nephritis. There are also statements which are debatable, such as the recommendations regarding investigation of all cases of acute urinary infection, the duration of chemotherapy for any urinary infection, and certain others. Its value would be enhanced if the titles of the references were included.

Despite these criticisms, it is a splendid contribution and should be a standard reference for all pediatricians and urologists.—*Harris D. Riley, Jr., M.D.*

GENETICS AND COUNSELING IN MEDICAL PRACTICE. By Leonard E. Reisman, M.D., Associate Professor of Pediatrics and Pathology, The Jefferson Medical College of Philadelphia, Philadelphia, Pennsylvania; and Adam P. Matheny, Jr., Ph.D., Assistant Professor of Pediatrics and Chief Psychologist, Children and Youth Project, University of Louisville School of Medicine, Louisville, Kentucky. 215 pp. with 86 illustrations. St. Louis: The C. V. Mosby Company, 1969. $12.75.

The authors state in the preface that the purpose of this book is to provide broad coverage of information that the family physician can use to help people seeking genetic advice. Genetic counseling certainly represents one of the major areas for clinical application of principles of medical genetics. Recognition and counseling of families at risk may lead not only to therapeutic but also preventive measures.

The authors, a pediatrician and a psychologist, have attempted to achieve their goal by providing 14 chapters in this monograph. However, some of the material is not

relevant to genetic counseling. Excessive space is given to style of counseling, timing and other details. On the other hand, certain topics which are closely related to genetic counseling have been omitted or are touched on only briefly, such as the problem of genetic heterogeneity.

Separate chapters explore common genetic abnormalities — their etiologies, consequences for the patient and appropriate counseling guidelines and approaches. A wide variety of diseases are covered.

The monograph begins with a chapter entitled "Overview," following which are chapters entitled "Clinical Tools for Genetic Counseling," "General Approach to Genetic Counseling" and "Probabilities in Genetic Counseling." Following this, the genetic aspects of a wide variety of disorders including congenital malformations, chromosomal abnormalities, inborn errors of metabolism,mental retardation and others are discussed.

This book will be of value to physicians concerned with this problem. Careful editing to eliminate certain inaccuracies would improve its effectiveness.—*Harris D. Riley, Jr., M.D.*

VIRAL ETIOLOGY OF CONGENITAL MALFORMATIONS. Proceedings of the Viral Etiology of Congenital Malformations Conference, May 19-20, 1967, National Institutes of Health, Bethesda, Maryland.

This is a small paperback volume which contains the edited transcript of the proceedings of a conference held at the National Institute of Child Health and Human Development in 1967. The object of the conference was to review the viral mechanisms of congenital malformations. There were 12 participants and seven visitors. The topics discussed are arranged under 12 headings, each having a short introduction. The subjects covered include the results to date in the perinatal research study done by the NIH, the functions of the placenta and virus infections of it, the immunological response of the fetus and epidemiologic approaches to etiologic problems. The volume is hampered by the absence of a subject index and of the literal translation of a great deal of conversational sections.—*Harris D. Riley, Jr., M.D.*

ATLAS OF MENTAL RETARDATION SYNDROMES: VISUAL DIAGNOSIS OF FACIES AND PHYSICAL FINDINGS. Sydney S. Gellis, M.D. and Murray Feingold, M.D. U.S. Department of Health, Education and Welfare. Washington: U.S. Government Printing Office. 188 pp. $5.50.

Many who have worked with the retarded and handicapped have felt the need for a reference work which would enable the clinician to more readily find a name for conditions of children with unusual appearance in order to find information about cases previously studied. This visual atlas, covering more than 80 syndromes, consists of a number of representative photographs (some in black and white, others in full color), capsule summaries of the major diagnostic features, the manifestations of mental retardation, the genetic aspects and managements. Clinical characteristics are indexed at the close of the text, followed by separate alphabetical index of syndrome names and synonyms.

Pediatricians and other physicians concerned with handicapped children will find this a valuable reference.—*Harris D. Riley, Jr., M.D.* □

Miscellaneous Advertisements

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DUE TO THE DEATH of one of our physicians, Logan County Hospital is seeking a G.P. to practice in Oakley, Kansas. Oakley is a community of 2,700, located along I-70 in Western Kansas. A beautiful community with all benefits of rural living. Possibilities of partnership available. Contact: Rodney Bates, Administrator, Logan County Hospital, Oakley, Kansas. 913 672-3211.

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GENERAL SURGEON, board certified or eligible. Immediate need for associate to live and practice in 1971 finalist All-American City. Locate or relocate . . . Contact Chas. R. Gibson, M.D., Chickasha Clinic, Inc. 224-4853. Inquiries kept confidential.

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Lincocin®

(lincomycin hydrochloride, Upjohn)

Up to 8 grams per day by IV infusion for hospitalized patients with life-threatening infections. Lincocin is effective in infections due to susceptible strains of streptococci, pneumococci, and staphylococci. As with all antibiotics, *in vitro* susceptibility studies should be performed.

Each preparation contains:	Lincomycin hydrochloride monohydrate equivalent to lincomycin base
250 mg Pediatric Capsule	250 mg
500 mg Capsule	500 mg
*Sterile Solution per 1 ml	300 mg
Syrup per 5 ml	250 mg

*Contains also: Benzyl Alcohol 9 mg; and, Water for Injection—q.s.

Lincocin (lincomycin hydrochloride) is indicated in infections due to susceptible strains of staphylococci, pneumococci, and streptococci. *In vitro* susceptibility studies should be performed. Cross resistance has not been demonstrated with penicillin, ampicillin, cephalosporins, chloramphenicol or the tetracyclines. Some cross resistance with erythromycin has been reported. Studies indicate that Lincocin does not share antigenicity with penicillin compounds.

CONTRAINDICATIONS: History of prior hypersensitivity to lincomycin or clindamycin. Not indicated in the treatment of viral or minor bacterial infections.

WARNINGS: *CASES OF SEVERE AND PERSISTENT DIARRHEA HAVE BEEN REPORTED AND HAVE AT TIMES NECESSITATED DISCONTINUANCE OF THE DRUG. THIS DIARRHEA HAS BEEN OCCASIONALLY ASSOCIATED WITH BLOOD AND MUCUS IN THE STOOLS AND HAS AT TIMES RESULTED IN AN ACUTE COLITIS. THIS SIDE EFFECT USUALLY HAS BEEN ASSOCIATED WITH THE ORAL DOSAGE FORM BUT OCCASIONALLY HAS BEEN REPORTED FOLLOWING PARENTERAL THERAPY.* A careful inquiry should be made concerning previous sensitivities to drugs or other allergens. Safety for use in pregnancy has not been established and Lincocin (lincomycin hydrochloride) is not indicated in the newborn. Reduce dose 25 to 30% in patients with severe impairment of renal function.

PRECAUTIONS: Like any drug, Lincocin should be used with caution in patients having a history of asthma or significant allergies. Overgrowth of nonsusceptible organisms, particularly yeasts, may occur and require appropriate measures. Patients with pre-existing monilial infections requiring Lincocin therapy should be given concomitant antimonilial treatment. During prolonged Lincocin therapy, periodic liver function studies and blood counts should be performed. Not recommended (inadequate data) in patients with pre-existing liver disease unless special clinical circumstances indicate. Continue treatment of β-hemolytic streptococci infections for 10 days to diminish likelihood of rheumatic fever or glomerulonephritis.

ADVERSE REACTIONS: *Gastrointestinal*—Glossitis, stomatitis, nausea, vomiting. Persistent diarrhea, enterocolitis, and pruritus ani. *Hemopoietic*—Neutropenia, leukopenia, agranulocytosis, and thrombocytopenic purpura have been reported. *Hypersensitivity reactions*—Hypersensitivity reactions such as angioneurotic edema, serum sickness, and anaphylaxis have been reported, sometimes in patients sensitive to penicillin. If allergic reaction occurs, discontinue drug. Have epinephrine, corticosteroids, and antihistamines available for emergency treatment. *Skin and mucous membranes*—Skin rashes, urticaria, vaginitis, and rare instances of exfoliative and vesiculobullous dermatitis have been reported. *Liver*—Although no direct relationship to liver dysfunction is established, jaundice and abnormal liver function tests (particularly serum transaminase) have been observed in a few instances. *Cardiovascular*—Instances of hypotension following parenteral administration have been reported, particularly after too rapid IV administration. Rare instances of cardiopulmonary arrest have been reported after too rapid IV administration. If 4.0 grams or more administered IV, dilute in 500 ml of fluid and administer no faster than 100 ml per hour. *Special senses*—Tinnitus and vertigo have been reported occasionally. *Local reactions*—Excellent local tolerance demonstrated to intramuscularly administered Lincocin (lincomycin hydrochloride). Reports of pain following injection have been infrequent. Intravenous administration of Lincocin in 250 to 500 ml of 5% glucose in distilled water or normal saline has produced no local irritation or phlebitis.

HOW SUPPLIED: *250 mg* and *500 mg* Capsules—bottles of 24 and 100. *Sterile Solution, 300 mg per ml*—2 and 10 ml vials and 2 ml syringe. *Syrup, 250 mg per 5 ml*—60 ml and pint bottles.

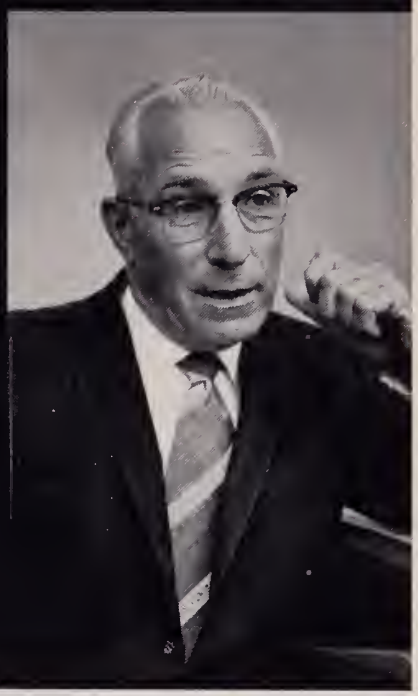
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When I look back at some of my old records, I'm constantly reminded of the changes that have come about in medicine just during the past twenty-five years. Some of the diseases I treated and prayed over in the '40's are found mostly in medical history books now.

Thanks to drug research and development, we've made substantial gains in the control of cardiovascular disease, diabetes, malaria, mental illness, strep and staph infections, meningitis and a long list of ailments. It seems like only yesterday when a diagnosis of pneumonia was almost the kiss of death. Now, with modern medical techniques and drug therapy, we can offer some real help.

My records on polio, influenza and measles show an unbelievable trend for the better. New vaccines have reduced the toll of these age-old threats dramatically. And I see patients in pain from crippling arthritis helped with new medicinals unknown just a few years ago.

I hear questions about the three billion or so dollars spent by the drug industry in research during the past ten years . . . working on new and better drug products. It does seem like quite a bit of money to spend, and I realize some of it goes into dead ends. That's the problem with research, any research . . . you often don't know where you're going until you get there. I want all the tools I can get to help my patients. I want more drugs and more effective drugs. If they mean less pain, longer lives and more productive careers for those I treat . . . well, that's what really counts.

Another point of view . . . Pharmaceutical Manufacturers Association, 1155 Fifteenth Street, N.W., Washington, D.C. 20005.

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Call it what you will, it may be premalignant...

Before

3/29/67 Before therapy with 5%-FU cream. Patient P. T. shows a moderately severe solar keratotic involvement. Note residual scarring from the previous cryosurgical and electrosurgical procedures on forehead and ridge of nose adjacent to periauricular area.

After

6/12/67 Seven weeks after cessation of therapy. Reactions have subsided. Residual scarring is not seen except for that due to prior surgery. Inflammation has disappeared and face is clear of keratotic lesions.



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and Efudex® (fluorouracil) 5% cream can resolve it.

Call it actinic, solar or senile keratoses, many regard it as "precancerous."[1,2]

Topical fluorouracil, considered by some dermatologists to be a major advance in the treatment of multiple solar keratoses,[3,4] offers the physician a relatively inexpensive alternative to cryosurgery, electrodesiccation and cold knife surgery. Of the topical fluorouracils available, only Efudex offers 2% and 5% solution and 5% cream formulations—formulations that have proved effective in the treatment of these mutliple lesions.

Usual duration of therapy, 2 to 4 weeks.

Studies showed that with the 2% and 5% Efudex preparations, the usual duration of therapy was only 2 to 4 weeks.[5] Other studies with topical fluorouracil revealed that when concentrations of less than 2% were used, significant numbers of lesions recurred.[6]

Treats the lesions you can't see, too.

Numerous lesions, not apparent prior to 2% and 5% Efudex therapy, manifested themselves by definite reactions, while intervening skin remained relatively unaffected.[5] The early eradication of these subclinical lesions (which may otherwise have undergone further progression) probably accounts for the reduced incidence of future solar keratoses in patients treated with topical fluorouracil—especially with 5% concentrations.[6]

How to identify solar keratoses.

Typically, the lesion—a flat or slightly elevated brown to red-brown papule—is dry, rough, adherent and sharply defined. Multiple lesions are the rule.

Predictable therapeutic response.

The response to a typical course of Efudex therapy is usually characteristic and predictable. After 3 or 4 days of treatment, erythema begins to appear in the area of keratoses. This is followed by a moderate to intense inflammatory response, scaling and occasionally moderate tenderness or pain. The height of this response generally occurs two weeks after the start of therapy and then begins to subside as treatment is stopped. Within two weeks of discontinuing medication, the inflammation is usually gone. Lesions that do not respond should be biopsied.

References: 1. Allen, A. C.: *The Skin, A Clinicopathological Treatise*, ed. 2, New York, Grune & Stratton, 1967, p. 842. 2. Dillaha, C. J.; Jansen, G. T, and Honeycutt, W. M.: "Treatment of Actinic Keratoses with Topical Fluorouracil," in Waisman, M. (ed.): *Pharmaceutical Therapeutics in Dermatology*, Springfield, Ill., Charles C Thomas, 1968, p. 92. 3. Belisario, J. C.: *Cutis, 6*:293, 1970. 4. Sams, W. M.: *Arch. Derm., 97*:14, 1968. 5. Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey. 6. Williams, A. C., and Klein, E.: *Cancer, 25*:450, 1970.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

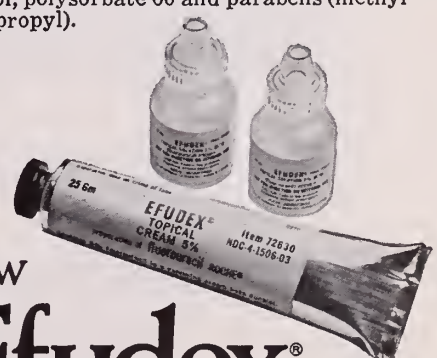
Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).



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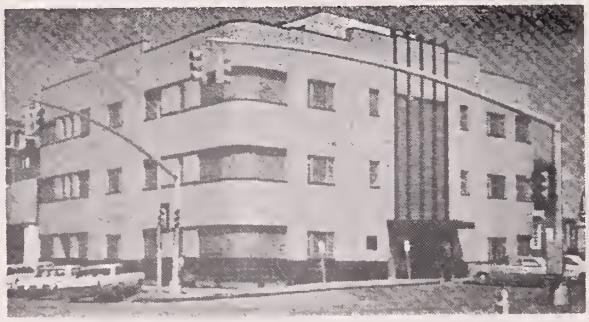
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The JOURNAL of the Oklahoma State Medical Association

DEADLINES

May Issue

Editorial, Scientific, Book Reviews — March 15, 1972
Advertiseing Copy — April 15, 1972
News Copy, Miscellaneous Ads — May 1, 1972

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Articles accepted for publication, including manuscripts of annual meeting papers, are the sole property of *The Journal* and must not have been published elsewhere. Authority for approval of all contributions rests with the Editorial Board, and the Board reserves the right to edit any material submitted. Manuscripts should be typewritten, double spaced and submitted in original and one copy. Receipt of manuscripts will be acknowledged and unused manuscripts returned. Used manuscripts will be returned on request. *The Journal of the Oklahoma State Medical Association* is not responsible for the statements or opinions of any contributor.

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NEWS

Members of the Oklahoma State Medical Association, the constituent societies of the association, and all readers in general are invited to supply news items of general interest to the profession.

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All advertising copy must be approved by the Editorial Board before acceptance for publication. General and miscellaneous advertising rates will be sent on request.

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Authors will receive reprint order forms from the Transcript Press, P.O. Drawer 1058, Norman, Oklahoma 73069, prior to final publication of their articles. Other requests for reprints must be made to the Transcript Press within 30 days after publication.

BACK ISSUES

Microfilm copies of back issues of *The Journal* may now be purchased from University Microfilms, 300 North Zeeb Road, Ann Arbor, Michigan 48106.

LEGISLATION—

WHOSE RESPONSIBILITY???

In the democratic process, the political power vested in each citizen not only represents an opportunity for involvement—it also carries a responsibility to become *involved!!!*

What are your plans for January 26th, 1972? Martha Hendren, Legislation chairman, has arranged a day at the State Capitol for us on that day. We hope to learn something of the KNOW HOW, WHO and WHY of what goes on in the inner sanctum of those walls.

Both branches of the Legislature will be represented at the workshop. We will be given the opportunity to question and visit with our own state senator and district representative. We can watch how the Senate and House conduct a day's session.

We must learn to be effective with our government by HOW to approach an issue —either for or against, WHOM to voice our approval or disapproval to. We should be well informed so we know WHY we do or do not support an issue, a candidate or an elected official.

At the present time, on the national level, there are about twenty bills in the Ways and Means Committee or in hearing that vitally affect every physician in practice. To be effective for Medicine (our chief business), we must be informed, we must work and we must speak out.

In his speech to the AMA House of Delegates in Atlantic City, President Nixon stated:

> "I know many of you are so concerned whenever anybody suggests that you get into politics and I do not speak in any partisan sense. I am not concerned about whether you are in politics in one party or the other. The main thing is to be in. I have heard a doctor say on occasion, 'I am only interested in my profession, I am not interested in politics.' Let me tell you something. He had better get interested in politics or he won't have any profession to be interested in."

Politics and legislation go hand-in-hand. Politics start on the local level. Come join us January 26th, 1972, State Capitol, Oklahoma City, 9:00 a.m. to 2:00 p.m.

Let's learn to be an effective, useful instrument for ourselves, our community and our profession. □

IF YOU DON'T REGISTER,

YOU CAN'T VOTE

OSMA JOURNAL / *the last word*

Phase II of President Nixon's Anti-Inflation Program has hit physicians. The Cost of Living Council's Price Commission has issued guidelines limiting physician fee increases to 2.5 percent. While the policy statement was issued in mid-December, the actual regulations were not published until early January. The news article appearing on page 31 of this issue of *The Journal* explains the Price Commission's actions as it was understood as of January 5th.

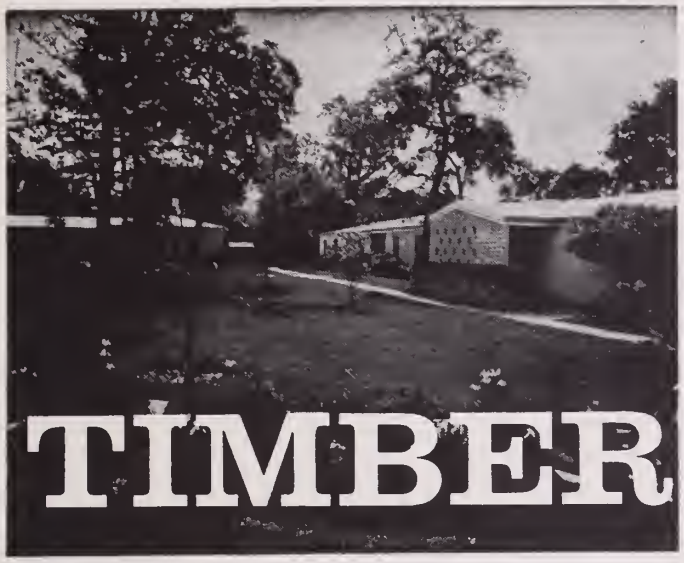
Washington observers are now speculating that Senator Russell Long (D-La.) may be planning to attach his stop-gap national health insurance proposal as an amendment to HR 1 (the Social Security Amendments of 1972). That bill is currently pending before the Senate Finance Committee which is chaired by the Senator. In early December Long proposed a sort of interim national health insurance plan consisting of adding the disabled to Medicare, catastrophic illness insurance protection, and expansion of Medicaid. His Finance Committee staff has been working on details of the plan while staying in close touch with Representative Wilbur Mills (D-Ark.), Chairman of the powerful House Ways and Means Committee. It is usually conceded that any NHI proposal must have the unified blessing of these two powerful members of congress.

A 40 percent reduction in physician manpower was announced by the Defense Department just a few days before a highly critical report of the Armed Services use of health professionals was issued by the General Accounting office. In a memorandum to the Assistant Secretaries for Manpower for each of the services, Richard S. Wilbur, M.D., Assistant Secretary of Defense, called for the substantial reductions by the end of 1972. His stated goal was to reduce the number of military physicians from 14,600 to 10,000. His announcement came just a few days before the GAO reported that the Armed Services are "wasting the talents of too many health professionals" on paperwork jobs. The report suggested that more than 200 physicians could be freed for patient care by using non-physicains as hospital commanders. This was one of the areas in which Wilbur recommended reductions. He also expressed the belief that the military services have more physicians than they need and that the military's medical needs can be met by increasing the efficiency of the medical corps. He pointed out that non-military physicians work about 56 hours a week and suggested that military physicians be given incentives to increase their patient loads. Such incentives could include higher pay and the opportunity to progress faster in rank.

Fee splitting for medical referrals, long declared unethical by the AMA, isn't tax deductible any more. One provision in the revenue act of 1971, approved by Congress in early December, provided that medical referral payments cannot be deducted from an individual's tax return as business expense. Section 7 of the AMA's Principles of Medical Ethics states, in pertinent part, " . . . he (the physician) should never pay nor receive a commission for referral of patients . . ." The Judicial Counsel of the AMA had stated that "A giving or receiving of a commission constitutes fee splitting and is unethical."

Four physicians have resigned from the Blue Shield Board of Trustees in response to the OSMA House of Delegates officially removing its endorsement of the plan. The four are Ed Calhoon, M.D., Beaver; Hillard Denyer, M.D., Bartlesville; C. Riley Strong, M.D., El Reno; and Joe Tyler, M.D., Tulsa. Scott Hendren, M.D., Oklahoma City, had previously announced that his term on the Board was ending and he would not accept reappointment. This leaves only four M.D.s of of the original nine on the Blue Shield Board.

A good public relations idea that may save a surgeon some medical-legal problems is to be sure to mention to the patient that there will be an assistant surgeon's fee. While surgeons ordinarily discuss their fee with a patient in advance of the surgery, they quite often forget to mention that there will be an assistant surgeon and that he will send a separate bill. Sometimes this advanced warning can soothe the savage patient. □



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Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. *Adults:* Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children:* 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

Supplied: Valium® (diazepam) Tablets, 2 mg, 5 mg and 10 mg; bottles of 100 and 500. All strengths also available in Tel-E-Dose™ packages of 1000.

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Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

Volume 65—Number 2—February 1972

JOURNAL
OKLAHOMA STATE MEDICAL ASSOCIATION



Before prescribing, please consult complete product information, a summary of which follows:

Indications: In adults, urinary tract infections complicated by pain (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli, Klebsiella-Aerobacter, Staphylococcus aureus, Proteus mirabilis,* and, less frequently, *Proteus vulgaris*) in the absence of obstructive uropathy or foreign bodies. *Important Note:* Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response. Add aminobenzoic acid to culture media for patients already taking sulfonamides. Increasing frequency of resistant organisms currently is a limitation of the usefulness of antibacterial agents. Blood levels should be measured in patients receiving sulfonamides for serious infections, since there may be wide variations with identical doses; 12 to 15 mg/100 ml is considered optimal for serious infections; 20 mg/100 ml should be the maximum total sulfonamide level, as adverse reactions occur more frequently above this level.

Contraindications: Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period. Contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with gastrointestinal disturbances, because of phenazopyridine HCl component.

Warnings: Safe use in pregnancy has not been established, and teratogenicity potential has not been thoroughly investigated. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported; clinical signs such as sore throat, fever, pallor, purpura or jaundice may be early indications of serious blood disorders. Complete blood counts and urinalysis with careful microscopic examination should be performed frequently during sulfonamide therapy.

Precautions: Use with caution in patients with impaired renal or hepatic function, severe allergy, bronchial asthma and in glucose-6-phosphate dehydrogenase-deficient individuals. In the latter, hemolysis, a frequently dose-related reaction, may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias:* agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia; *allergic reactions:* erythema multiforme (Stevens-Johnson syndrome), skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis; *gastrointestinal reactions:* nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis; *C.N.S. reactions:* headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia; and *miscellaneous reactions:* drug fever, chills, toxic nephrosis with oliguria and anuria, polyarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide and thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

Dosage: Usual adult dosage for acute, painful phase of urinary tract infection is 4 tablets initially, then 2 tablets morning and evening. If pain persists beyond seven days, causes other than infection should be sought. After relief has been obtained, continued treatment with Gantanol (sulfamethoxazole) may be considered.

NOTE: Patients should be told that the orange-red dye (phenazopyridine HCl) will color the urine soon after ingestion.

How Supplied: Tablets, each containing 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl, bottles of 100 and 500.

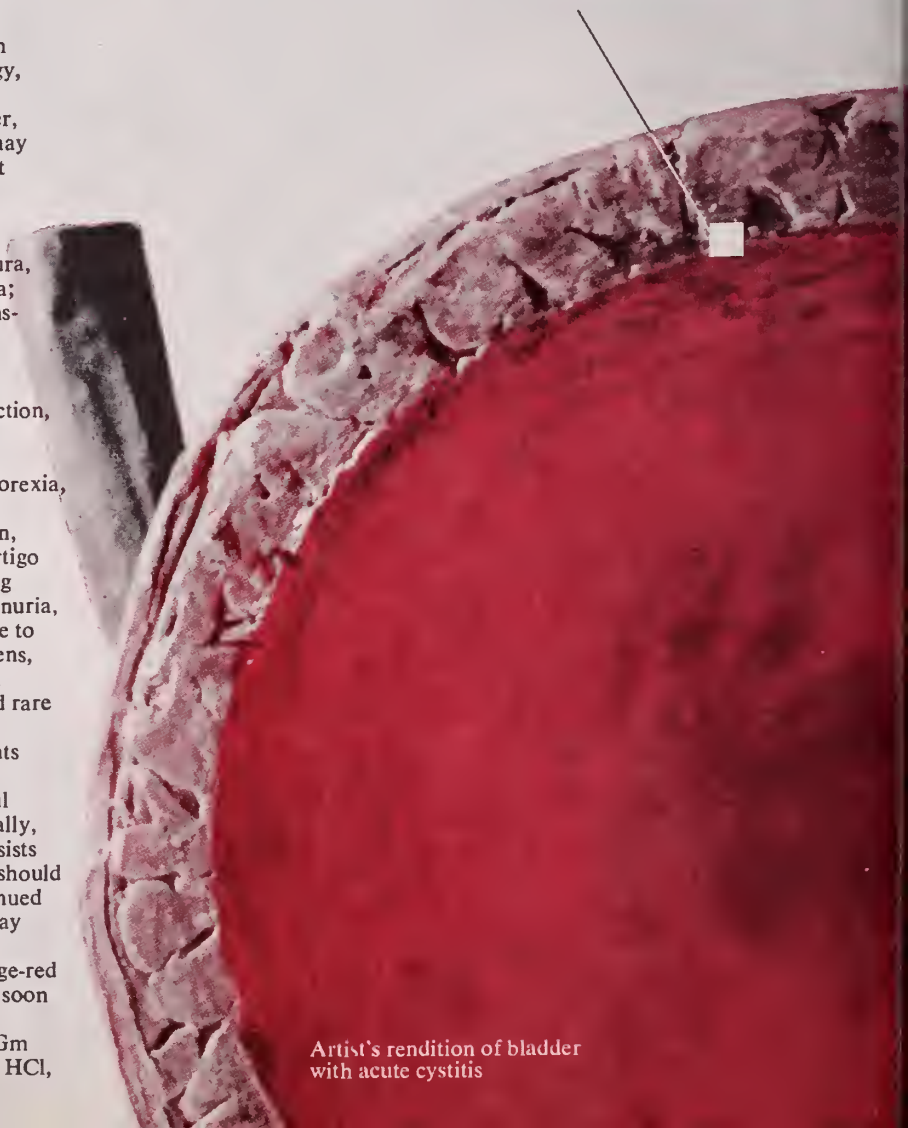
Azo

Each tablet contains 100 mg phenazopyridine H

for dramatic relief from symptoms within minutes



Artist's rendition of inflamed mucosa of the bladder wall

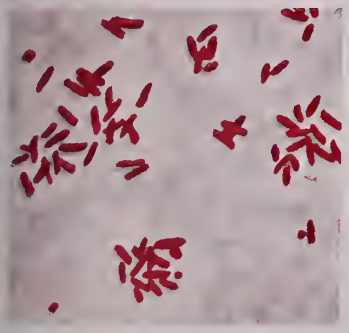


Artist's rendition of bladder with acute cystitis

Gantanol®

0.5 Gm sulfamethoxazole.

for effective antibacterial action within hours



Artist's rendition of *E. coli*

Rapid relief of discomfort

The patient needs prompt relief of urinary bladder pain and the physician needs to initiate early antibacterial action to fight the infection. This is where the basic therapy of dual-action Azo Gantanol® can help... the analgesic action of Azo (phenazopyridine HCl) for prompt relief from bladder pain and the effective action of Gantanol® (sulfamethoxazole) to control the bladder infection.

Antibacterial blood/urine levels in from 2 to 3 hours

With the initial 2-Gm dose, the analgesic action of the Azo component starts immediately to relieve the symptoms associated with an infected and inflamed bladder. In from 2 to 3 hours, as effective antibacterial blood and urine levels are reached, the Gantanol action begins to control the bacteria most often implicated in acute infections of the bladder . . . susceptible *E. coli* as well as susceptible strains of *Klebsiella-Aerobacter, Staph. aureus, Proteus mirabilis,* and, less frequently, *P. vulgaris*. The usual precautions in sulfonamide therapy, including maintenance of adequate fluid intake, should be observed. The most common side effects are nausea, vomiting and diarrhea.

12 hours of therapy with every dose

Subsequent *b.i.d.* doses of 1 Gm, morning and evening, maintain effective antibacterial coverage on a round-the-clock basis. With every dose, Azo Gantanol helps relieve the symptoms of cystitis while it fights the infection.



In acute painful nonobstructed cystitis

Azo Gantanol®

Each tablet contains 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl.

basic therapy

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The JOURNAL of the Oklahoma State Medical Association

FEBRUARY 1972
Vol. 65, No. 2

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Arthur lost



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his pinworms...



with just one non-staining dose of Antiminth (pyrantel pamoate) Oral Suspension.

Highly effective. Active against pinworm...and roundworm.

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Pleasant-tasting. Easy-to-take, caramel-flavored oral suspension.

Economical. One prescription for the entire family.

Antiminth (pyrantel pamoate) Oral Suspension

Actions. Antiminth (pyrantel pamoate) has demonstrated anthelmintic activity against *Enterobius vermicularis* (pinworm) and *Ascaris lumbricoides* (roundworm). The anthelmintic action is probably due to the neuromuscular blocking property of the drug.

Antiminth is partially absorbed after an oral dose. Plasma levels of unchanged drug are low. Peak levels (0.05-0.13 μg/ml) are reached in 1-3 hours. Quantities greater than 50% of administered drug are excreted in feces as the unchanged form, whereas only 7% or less of the dose is found in urine as the unchanged form of the drug and its metabolites.

Indications. For the treatment of ascariasis (roundworm infection) and enterobiasis (pinworm infection).

Warnings. *Usage in Pregnancy:* Reproduction studies have been performed in animals and there was no evidence of propensity for harm to the fetus. The relevance to the human is not known.

There is no experience in pregnant women who have received this drug.

Precautions. Minor transient elevations of SGOT have occurred in a small percentage of patients. Therefore, this drug should be used with caution in patients with pre-existing liver dysfunction.

Adverse Reactions. The most frequently encountered adverse reactions are related to the gastrointestinal system.

Gastrointestinal and hepatic reactions: anorexia, nausea, vomiting, gastralgia, abdominal cramps, diarrhea and tenesmus, transient elevation of SGOT.

CNS reactions: headache, dizziness, drowsiness, and insomnia.

Skin reactions: rashes.

Dosage and Administration. *Children and Adults:* Antiminth Oral Suspension (50 mg. of pyrantel base/ml.) should be administered in a single dose of 11 mg. of pyrantel base per kg. of body weight (or 5 mg./lb.); maximum total dose 1 gram. This corresponds to a simplified dosage regimen of 1 cc. of Antiminth per 10 lbs. of body weight. (One teaspoonful = 5 cc.)

Antiminth (pyrantel pamoate) Oral Suspension may be administered without regard to ingestion of food or time of day; and purging is not necessary prior to, during, or after therapy. It may be taken with milk or fruit juices. Because of limited data on repeated doses, no recommendations can be made.

How Supplied. Antiminth is available as a pleasant tasting caramel-flavored suspension which contains the equivalent of 50 mg. pyrantel base per ml., supplied in 60 cc. bottles.

gent: **new ANTIMINTH®**
(pyrantel pamoate)
equivalent to 50 mg pyrantel/ml
ORAL SUSPENSION

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400 mg tablets

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Pre-Sate® (chlorphentermine hydrochloride)

Caution: Federal law prohibits dispensing without prescription.

Indications
Pre-Sate (chlorphentermine hydrochloride) is indicated in exogenous obesity, as a short term (i.e. several weeks) adjunct in a regimen of weight reduction based upon caloric restriction.

Contraindications
Glaucoma, hyperthyroidism, pheochromocytoma, hypersensitivity to sympathomimetic amines, and agitated states. Pre-Sate (chlorphentermine hydrochloride) is also contraindicated in patients with a history of drug abuse or symptomatic cardiovascular disease of the following types: advanced arteriosclerosis, severe coronary artery disease, moderate to severe hypertension, or cardiac conduction abnormalities with danger of arrhythmias. The drug is also contraindicated during or within 14 days following administration of monamine oxidase inhibitors, since hypertensive crises may result.

Warnings
When weight loss is unsatisfactory the recommended dosage should not be increased in an attempt to obtain increased anorexigenic effect, discontinue the drug. Tolerance to the anorectic effect may develop. Drowsiness or stimulation may occur and may impair ability to engage in potentially hazardous activities such as operating machinery, driving a motor vehicle, or performing tasks requiring precision work or critical judgment. Therefore, such patients should be cautioned accordingly. Caution must be exercised if Pre-Sate (chlorphentermine hydrochloride) is used concomitantly with other central nervous system stimulants. There have been reports of pulmonary hypertension in patients who received related drugs.

Drug Dependence Drugs of this type have a potential for abuse. Patients have been known to increase the intake of drugs of this type to many times the dosages recommended. In long-term controlled studies with the high dosages of Pre-Sate, abrupt cessation did not result in symptoms of withdrawal.

Usage In Pregnancy The safety of Pre-Sate (chlorphentermine hydrochloride) in human pregnancy has not yet been clearly established. The use of anorectic agents by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and child. Use of the drug during lactation is not recommended. Mammalian reproductive and teratogenic studies with high multiples of the human dose have been negative.

Usage In Children Not recommended for use in children under 12 years of age.

Precautions
In patients with diabetes mellitus there may be alteration of insulin requirements due to dietary restrictions and weight loss. Pre-Sate (chlorphentermine hydrochloride) should be used with caution when obesity complicates the management of patients with mild to moderate cardiovascular disease or diabetes mellitus, and only when dietary restriction alone has been unsuccessful in achieving desired weight reduction. In prescribing this drug for obese patients in whom it is undesirable to introduce CNS stimulation or pressor effect, the physician should be alert to the individual who may be overly sensitive to this drug. Psychologic disturbances have been reported in patients who concomitantly receive an anorectic agent and a restrictive dietary regimen.

Adverse Reactions
Central Nervous System: When CNS side effects occur, they are most often manifested as drowsiness or sedation or overstimulation and restlessness. Insomnia, dizziness, headache, euphoria, dysphoria, and tremor may also occur. Psychotic episodes, although rare, have been noted even at recommended doses. **Cardiovascular:** tachycardia, palpitation, elevation of blood pressure. **Gastrointestinal:** nausea and vomiting, diarrhea, unpleasant taste, constipation. **Endocrine:** changes in libido, impotence. **Autonomic:** dryness of mouth, sweating, mydriasis. **Allergic:** urticaria. **Genitourinary:** diuresis and, rarely, difficulty in initiating micturition. **Others:** Paresthesias, sural spasms.

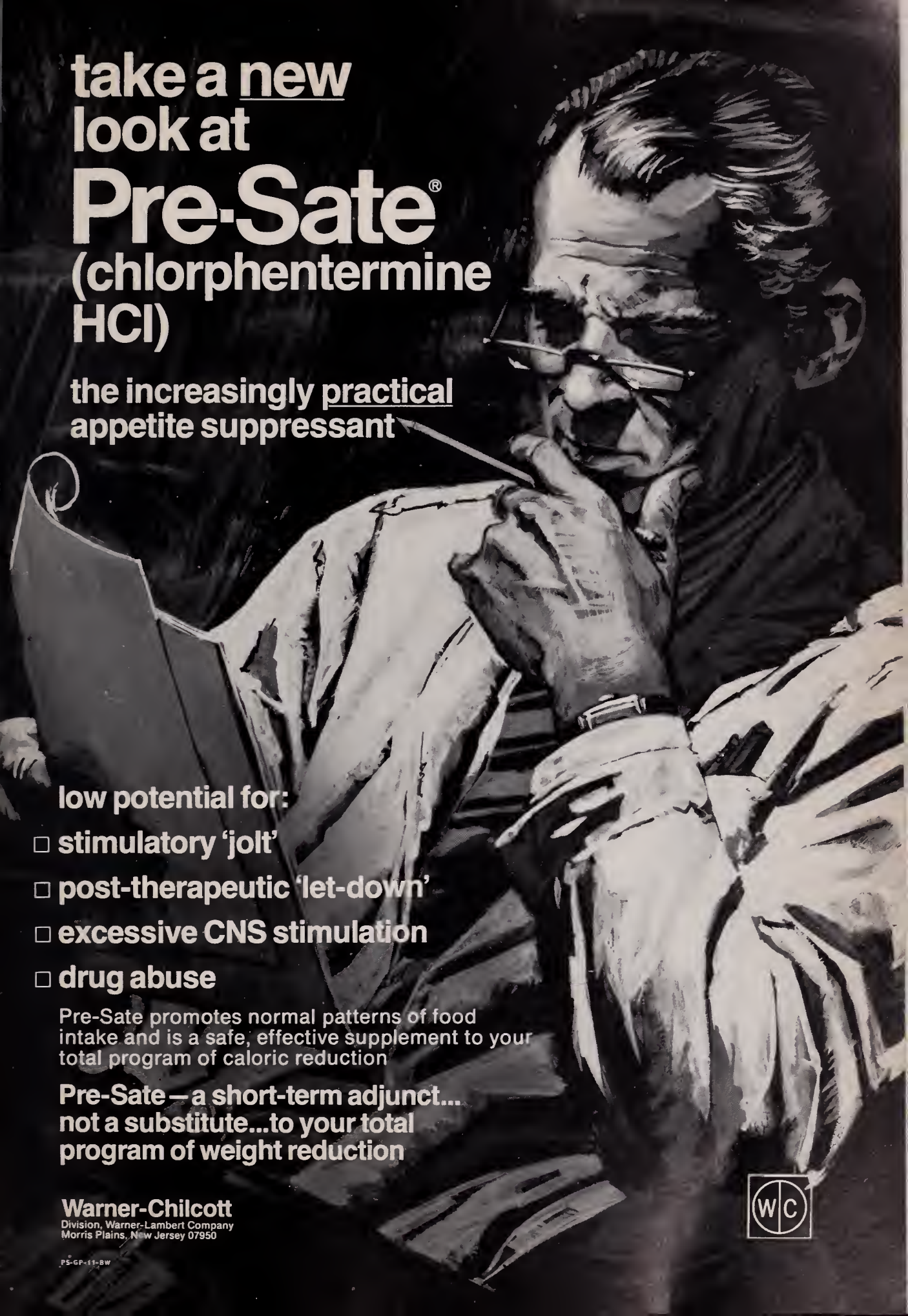
Dosage and Administration
The recommended adult daily dose of Pre-Sate (chlorphentermine hydrochloride) is one tablet (equivalent to 65 mg chlorphentermine base) taken after the first meal of the day. Use in children under 12 not recommended.

Overdosage
Manifestations: Restlessness, confusion, assaultiveness, hallucinations, panic states, and hyperpyrexia may be manifestations of acute intoxication with anorectic agents. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension, or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.

Management: Management of acute intoxication with sympathomimetic amines is largely symptomatic and supportive and often includes sedation with a barbiturate. If hypertension is marked, the use of a nitrate or rapidly acting alpha-receptor blocking agent should be considered. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard.

How Supplied
Each Pre-Sate (chlorphentermine hydrochloride) tablet contains the equivalent of 65 mg chlorphentermine base; bottles of 100 and 1000 tablets.

Full information is available on request.


take a new look at
Pre-Sate®
(chlorphentermine HCl)
the increasingly practical appetite suppressant
low potential for:
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□ excessive CNS stimulation
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WC



When you select this familiar antibiotic for IV infusion you have available a broad dosage range that hospitalized patients may need.

Intravenous Lincocin (lincomycin hydrochloride, Upjohn), with its 1.2 to 8 grams/day dosage range, covers many serious and even life-threatening infections. Lincocin is effective in infections due to susceptible strains of streptococci, pneumococci, and staphylococci. Lincocin IV therefore can be as useful in your hospitalized patients as its IM use has proved to be in your office patients. As with all antibiotics, *in vitro* susceptibility studies should be performed.

1.2 to 8 grams/day IV dosage range: Most hospitalized patients with uncomplicated pneumonias respond satisfactorily to 1.2 to 1.8 grams/day of Lincocin IV. These doses may have to be increased for more serious infections. In life-threatening situations as much as 8 grams/day has been administered intravenously to adults.

In usual IV doses, Lincocin (lincomycin hydrochloride, Upjohn) should be diluted in 250 ml or more of normal saline solution or 5% glucose in water. But when 4 grams or more per day is given, Lincocin should be diluted in not less than 500 ml of either solution, and the rate of administration should not exceed 100 ml/hour. Too rapid intravenous administration of doses exceeding 4 grams may result in hypotension or, in rare instances, cardiopulmonary arrest.

Effective gram-positive antibiotic: Lincocin IV is effective in respiratory tract, skin and soft-tissue, and bone

infections caused by susceptible strains of pneumococci, streptococci, and staphylococci, including penicillin-resistant strains. Staphylococcal strains resistant to Lincocin (lincomycin hydrochloride, Upjohn) have been recovered. Before initiating therapy, culture and susceptibility studies should be performed. Lincocin has proved valuable in treating patients hypersensitive to penicillin or cephalosporins, since Lincocin does not share antigenicity with these compounds. However, hypersensitivity reactions have been reported, some of these in patients known to be sensitive to penicillin.

Well tolerated at infusion site: Lincocin intravenous infusions have not produced local irritation or phlebitis, when given as recommended. Lincocin is usually well tolerated in patients who are hypersensitive to other drugs. Nevertheless, Lincocin should be used cautiously in patients with asthma or significant allergies.

In patients with impaired renal function, the recommended dose of Lincocin should be reduced to 25—30% of the dose for patients with normal kidney function. Its safety in pregnant patients and in infants less than one month of age has not been established.

Lincocin may be used with other antimicrobial agents: Since Lincocin is stable over a wide pH range, it is suitable for incorporation in intravenous infusions; it also may be administered concomitantly with other antimicrobial agents when indicated. However, Lincocin should not be used with erythromycin, as *in vitro* antagonism has been reported.

Lincocin®

Sterile Solution (300 mg per ml)

(lincomycin hydrochloride, Upjohn)

For further prescribing information, please see following page.



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Sterile Solution (300 mg. per ml.)

Lincocin®

(lincomycin hydrochloride, Upjohn)

Up to 8 grams per day by IV infusion for hospitalized patients with life-threatening infections. Lincocin is effective in infections due to susceptible strains of streptococci, pneumococci, and staphylococci. As with all antibiotics, *in vitro* susceptibility studies should be performed.

Each preparation contains:	Lincomycin hydrochloride monohydrate equivalent to lincomycin base
250 mg Pediatric Capsule	250 mg
500 mg Capsule	500 mg
*Sterile Solution per 1 ml	300 mg
Syrup per 5 ml	250 mg

*Contains also: Benzyl Alcohol 9 mg; and, Water for Injection—q.s.

Lincocin (lincomycin hydrochloride) is indicated in infections due to susceptible strains of staphylococci, pneumococci, and streptococci. *In vitro* susceptibility studies should be performed. Cross resistance has not been demonstrated with penicillin, ampicillin, cephalosporins, chloramphenicol or the tetracyclines. Some cross resistance with erythromycin has been reported. Studies indicate that Lincocin does not share antigenicity with penicillin compounds.

CONTRAINDICATIONS: History of prior hypersensitivity to lincomycin or clindamycin. Not indicated in the treatment of viral or minor bacterial infections.

WARNINGS: *CASES OF SEVERE AND PERSISTENT DIARRHEA HAVE BEEN REPORTED AND HAVE AT TIMES NECESSITATED DISCONTINUANCE OF THE DRUG. THIS DIARRHEA HAS BEEN OCCASIONALLY ASSOCIATED WITH BLOOD AND MUCUS IN THE STOOLS AND HAS AT TIMES RESULTED IN AN ACUTE COLITIS. THIS SIDE EFFECT USUALLY HAS BEEN ASSOCIATED WITH THE ORAL DOSAGE FORM BUT OCCASIONALLY HAS BEEN REPORTED FOLLOWING PARENTERAL THERAPY.* A careful inquiry should be made concerning previous sensitivities to drugs or other allergens. Safety for use in pregnancy has not been established and Lincocin (lincomycin hydrochloride) is not indicated in the newborn. Reduce dose 25 to 30% in patients with severe impairment of renal function.

PRECAUTIONS: Like any drug, Lincocin should be used with caution in patients having a history of asthma or significant allergies. Overgrowth of nonsusceptible organisms, particularly yeasts, may occur and require appropriate measures. Patients with pre-existing monilial infections requiring Lincocin therapy should be given concomitant antimonilial treatment. During prolonged Lincocin therapy, periodic liver function studies and blood counts should be performed. Not recommended (inadequate data) in patients with pre-existing liver disease unless special clinical circumstances indicate. Continue treatment of β-hemolytic streptococci infections for 10 days to diminish likelihood of rheumatic fever or glomerulonephritis.

ADVERSE REACTIONS: *Gastrointestinal*—Glossitis, stomatitis, nausea, vomiting. Persistent diarrhea, enterocolitis, and pruritus ani. *Hemopoietic*—Neutropenia, leukopenia, agranulocytosis, and thrombocytopenic purpura have been reported. *Hypersensitivity reactions*—Hypersensitivity reactions such as angioneurotic edema, serum sickness, and anaphylaxis have been reported, sometimes in patients sensitive to penicillin. If allergic reaction occurs, discontinue drug. Have epinephrine, corticosteroids, and antihistamines available for emergency treatment. *Skin and mucous membranes*—Skin rashes, urticaria, vaginitis, and rare instances of exfoliative and vesiculobullous dermatitis have been reported. *Liver*—Although no direct relationship to liver dysfunction is established, jaundice and abnormal liver function tests (particularly serum transaminase) have been observed in a few instances. *Cardiovascular*—Instances of hypotension following parenteral administration have been reported, particularly after too rapid IV administration. Rare instances of cardiopulmonary arrest have been reported after too rapid IV administration. If 4.0 grams or more administered IV, dilute in 500 ml of fluid and administer no faster than 100 ml per hour. *Special senses*—Tinnitus and vertigo have been reported occasionally. *Local reactions*—Excellent local tolerance demonstrated to intramuscularly administered Lincocin (lincomycin hydrochloride). Reports of pain following injection have been infrequent. Intravenous administration of Lincocin in 250 to 500 ml of 5% glucose in distilled water or normal saline has produced no local irritation or phlebitis.

HOW SUPPLIED: *250 mg* and *500 mg* Capsules—bottles of 24 and 100. *Sterile Solution, 300 mg per ml*—2 and 10 ml vials and 2 ml syringe. *Syrup, 250 mg per 5 ml*—60 ml and pint bottles.

For additional product information, consult the package insert or see your Upjohn representative.

MED B-6-S (KZL-7) JA71-1631

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Kalamazoo, Michigan 49001

Upjohn



rheumatoid arthritic blowup...

Tandearil® Geigy

oxyphenbutazone NF

tablets of 100 mg.

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral lesions (symptoms of blood dyscrasia); dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.
Indications: Acute gouty arthritis, rheumatoid arthritis, rheumatoid spondylitis.
Contraindications: Children 14 years or less; senile patients; history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypertension; thyroid disease; systemic edema; stomatitis and salivary gland enlargement due to the drug; polymyalgia rheumatica and temporal arteritis; patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.
Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpredictable benefits against potential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.
Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.
Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angiitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement.
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Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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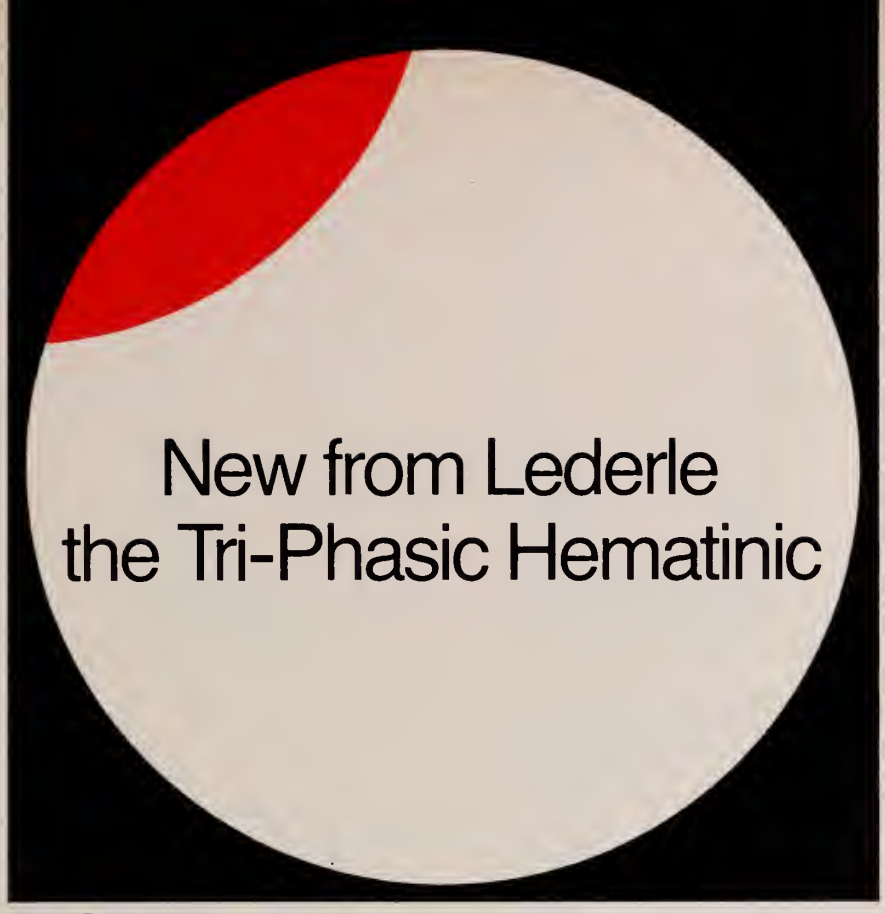
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Charles F. Kettering--A Portrait

ONE OF THE many satisfactions in the practice of medicine is the privileged opportunity one has to know, to understand and appreciate people. Perhaps more than any other profession, we physicians have an entree to the real character of people. We meet them from all walks of life, on a plane relatively free of sham or commercial pressures and with an aim of mutual understanding. Though at times we may become preoccupied with the anatomy of a patient's illness, usually the patient himself is at least as interesting and memorable as his disease. I believe that most of us will agree that our personal as well as professional lives are often shaped profoundly by these human contacts.

Each of us could come up with his own gallery of portraits. One unforgettable character whom I was privileged to know, first as a patient and then as a close personal friend over the last decade of his life, was Charles F. Kettering. Though not a physician, he contributed vastly more to medicine than most of us within the profession can aspire to. His name is perhaps best known to us today for the philanthropic contributions which he made to research and patient care. However he left also a bequest in the form of his personal qualities: His pragmatism, his many aphorisms which reflect an earthy, simple and objective approach to even complex problems, his downright wisdom and the inveterate spirit of adventure and wonderment which he maintained to the end of a very active life. These personal traits were best known to a few with whom he was closely associated at General Motors and only now and then did they sparkle through in a public interview or writing.

Especially applicable today, I believe, are his comments about research, which was his lifelong pursuit, and these are as relevant to medicine as to engineering. Some of them are included in a little tribute which I wrote on the occasion of his death thirteen years ago.

Medicine has had few more devoted patrons and co-workers than Charles Franklin Kettering. "Boss Ket," as he was affectionately known to the thousands of people of General Motors, was an engineer whose contributions to the automotive age (the self starter, ethyl gasoline, high compression engines, diesel locomotives) won him renown as an inventor and a fortune estimated at many millions. A large share of that fortune, and also of his life, he devoted to medical research.

Writing on the occasion of the seventy-fifth anniversary of the American Medical Association he summed up the sense of kinship he felt for our profession: ". . . we must break down the boundaries between engineering and medicine . . . all of us, all the professions, are a part of one big work banding together to fight for every form of human progress.[2] He rebelled against pedagogical boundaries and the vocabularies of scientific jargon which separate workers with a common cause. His own achievements ranged through the fields of physics, chemistry and biology, in addition to his own. From his years of close association with physicians he learned much of medicine. And medicine can learn much from him.

"The Boss" had a genius for going to the core of a problem or an idea, reducing it to its least common denominator, and crystallizing his thoughts into "Ketteringisms" that reveal his pragmatist's philosophy. "In research the hard thing to recognize is that the problem you are working on is boss." Making a plea for an educational system which would teach students to "fail intellectually" he pointed out that "an inventor fails 999 times and if he succeeds once he's in." Most important, "the one time you don't want to fail is the last time you try."

If "Boss Ket" had a hobby it was debunking dogmas. "It isn't what we don't know that holds so much as the things we know for sure that are not so." He made a sharp distinction between formal education and learning. "Real progress," he believed, "is made by those who are quite different from educated people. Facing an inscrutable disease, the men who make progress do so be-

(Continued on Page 75)



As your President, I was privileged to serve as "Doctor of the Day" at the opening of the second session of the 33rd Oklahoma Legislature. And as a Radiologist, I had the opportunity to relive for a moment a segment of my past as a general practitioner. On this occasion also, I heard the governor's message to the combined houses of the Legislature.

Of major interest to our profession is the governor's thinking on health issues. Considerable emphasis was laid on rural and urban development, availability and delivery of the best health care, acquisition of adequate allied health manpower and improved transportation between rural areas and regional and metropolitan health facilities as a bonus of his commitment to "Freeway—77," a $250 million dollar highway bond program. Proposed legislation to prohibit importation and sale of amphetamines has already resulted in division of opinion among the medical profession. The intent to eliminate amphetamine abuse is laudable but the wisdom of furthering more governmental control is questionable. Nonetheless, I feel that our profession is in general accord with the governor's health proposals and will offer its cooperation.

The first meeting of the Legislative Committee was held on January 23rd, 1972. Support was voted for the following: An act "for recognition of physicians' assistants, their certification, and vesting authority for promulgation of rules and regulations in the State Board of Medical Examiners," removal of age of consent for examination and treatment by a licensed physician, and an act "establishing the Tulsa Medical School, a branch program operation of the University of Oklahoma School of Medicine to be located in Tulsa County," placing amphetamines, ritalin and pentozocine in Schedule II of Public Law 91-513 concerned with controlled substances and establishment of requirements for examination and treatment by a licensed physician, establishing requirements for applicants to be licensed in the healing arts to be graduates of medical schools accredited by the U.S. Office of Education and for those licensed as general practitioners of the healing arts to pass a basic science exam equivalent to Oklahoma's examination.

Opposition by the committee was directed to the following: Senate Bill Number 458, an act to be known as the "Uniform Abortion Act of Oklahoma"—opposed as written and to be submitted to the Board of Trustees for their position, an act prohibiting the importation and distribution of amphetamines, an act relating to establishing a Board of Chiropractic Examiners and a method of licensing chiropractic applicants. Other bills failing to receive support included requiring health insurers to pay for the services of all practitioners of the healing arts at the request of the insured, to require every hospital in the state to admit emergency patients for treatment for at least 48 hours, to levy an annual tax on insurance premiums, and to require insurance companies to add the service of chiropractors to their health policies.

It is obvious that all bills to be submitted cannot be enumerated. Some will be of more interest and importance than others. One can be assured that a busy session is promised on the medical front and it behooves each of us to study these bills and be prepared to make our opinions individually and collectively known to our representatives in the Legislature. □

Sincerely,

Lucien H. Pascuzzi

OSMA JOURNAL/scientific

Thalidomide Revisited

GERALD M. ROBERTSON, MD

The history and disastrous consequences of thalidomide are known; however, little is known of its mechanism of action. Some hypotheses are presented.

THALIDOMIDE was first synthesized in Germany in 1953 and was initially tried as an anticonvulsant on human subjects. It proved to have hypnotic and sedative properties which had not been demonstrated in prior animal studies. The drug was available in Germany without prescription for some time; however, in 1959 manufacturers suggested that it be made available only on prescription basis because of reports of peripheral neuritis in patients who had taken the drug over a period of time.[1]

Two American drug companies investigated thalidomide in 1956-57 but subsequently lost interest. Investigation again occurred in 1959, and thalidomide was subjected to clinical trial as a hypnotic and sedative until December 1961, at which time it was withdrawn from human use virtually worldwide.[1]

STRUCTURE

The effects of thalidomide (α - (N-phthalimido) glutarimide or N-2,6-dioxo-3-piperidyl phthalimide) have been the subject of extensive research. Thalidomide differs from other known sedatives in its chemical structure, pharmacological activity, and toxicological properties.

When examining the structural formula of thalidomide (Figure 1) and comparing it

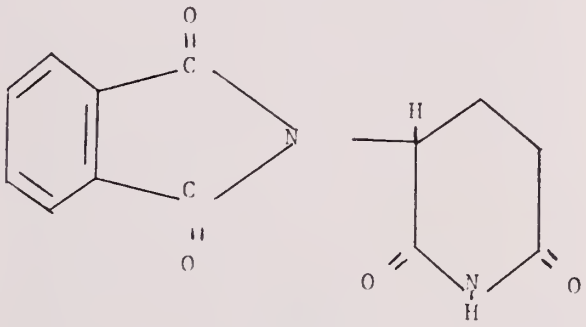


Figure 1

with the structural formulae of other known sedatives (barbituric acids, piperidines,, piperizines, morpholines, diazines, trizines, and many others), one notices that in the α position of thalidomide is an acylated amino group instead of two hydrocarbon residues which occur in the more common sedatives. Thalidomide is the only known sedative to be derived from a natural endogenous α-amino acid (glutamic acid).[2]

ACTIVITY

In addition to structure, the pharmacological properties of thalidomide also differ from the properties of other known hypnotics, sedatives, and anticonvulsive agents. In animal experiments thalidomide was found to be a mild sedative which rapidly reduced movement spontaneity without interfering with movement coordination.[3,4] Unlike most other sedatives, thalidomide, when taken in extreme overdosage, produced no anaesthetic effects in man.[5] Cases were reported in which two pregnant women attempted suicide by taking several thalidomide doses of 700mgm per dose with no anaesthetic effects.[6] The fact that thalidomide is only sparingly soluble in water does not adequately explain this low toxicity phenomenon, for a considerable amount of the thalidomide intake is absorbed.[7]

TOXICITY

During the early 1960's, many reports on the suspected teratogenic effects of thalidomide were published. The reported congenital abnormalities seemed to follow a general pattern with the following characteristics in common:

1. Mostly symmetrical defects
2. Preponderance of defects in upper limbs
3. Lower limbs affected, but to a lesser degree
4. More serious malformation preponderate in girls.

Other anomalies less frequently present were: Lesions of the alimentary tract, absence or deformity of the external arms, failure of the fetal fissure of the embryonic eye to close, and various cardiac abnormalities. The defects involving the limbs are characterized by the presence of extremities on the trunk, e.g., hands joined to shoulders with the absence of arms. The word "Phocomelia" (Greek: *phoke* - seal; *melos* - limb) is commonly used to describe the affliction.

METABOLISM

As the circumstantial evidence mounted against thalidomide as being the teratogenic agent,[8] investigations were undertaken to elucidate the exact mechanisms by which the congenital malformations were produced.

Barrow, Steffek and King treated three gravid rhesus monkeys (*Macaca mulatta*) with varying amounts of thalidomide. They stated, "Not only is administration during a critical and early time period necessary for the development of severe and complete phocomelia in the rhesus monkey, but an impressively low dosage of the compound is needed to achieve this end."[9]

In order to study thalidomide metabolism, Faigle, Keberle, Riess, and Schmid synthesized radioactive thalidomide by a process in which the C^{14} molecules were in the phthalic acid portion of the thalidomide produced. This method was chosen, for if thalidomide undergoes cleavage, it would still be possible to trace the exogenous phthalic acid or its derivatives. The resulting compound is shown below:[2]

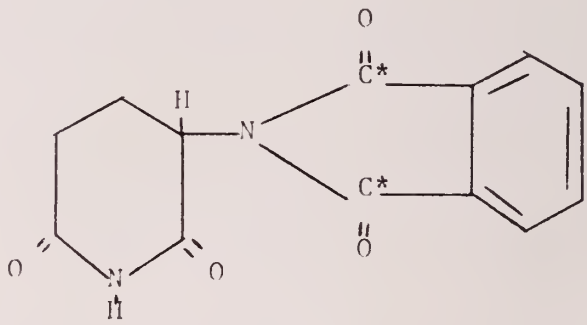


Figure 2

The C^{14} -thalidomide was orally administered to albino rats and to dogs in varying dosages. It was concluded by measuring the radioactivity of the exhaled air that no radical degradation or decarboxylation occurred in the phthalic acid portion of the molecule. The animals were sacrificed at various time intervals, and their various organs were examined to determine the relative concentration of the radioactivity of each organ. The data showed thalidomide to be more or less evenly distributed throughout the body organs with higher concentrations being encountered in the gastrointestinal tract and in the kidneys. The maximum thalidomide concentration was obtained after about four hours. It was also demonstrated that, after thalidomide administration had ceased, the concentration of this drug (or a radioactive

metabolite) left the formed elements of the blood at a very slow rate. Thalidomide was also shown to be able to cross the placental barrier, for the thalidomide concentration in homogenized new-born rats was the same as that of the mother.[2]

The presence of thalidomide in the embryo was also demonstrated by Fabro, Schumacher, Smith, and Williams. Pregnant rabbits were administered 6mg/kg of C^{14} -thalidomide in the tenth day of pregnancy and were sacrificed four hours later. Thalidomide was concentrated chiefly in the liver of the adult rabbits—three to four times the amount found in the blood. In the blastocysts, 90 percent of the activity present was in the yolk sac, and the other ten percent was found to be in the yolk sac membrane and embryo.[10]

Dogs were fed 100mgm/kg of C^{14} -thalidomide daily for ten days. The urine accounted for 27.9 percent of the administered dose; the remainder was excreted in the feces. (All fecal activity was accounted for by unchanged thalidomide.) Ninety-five percent of the urinary activity was found to be in the form of phthalic acid.[2] These findings suggested that the metabolites of thalidomide *in vivo* were formed only by simple hydrolysis of amide links and hydroxylation of the aromatic ring.[11] It was found later that thalidomide spontaneously decomposes at physiological pH values to give rise to several urinary metabolites.[12]

R. T. Williams suggested (from fluorescence studies and chromatography) that thalidomide urine from rats, rabbits, and man contained hydroxy compounds derived from thalidomide and related to 3-hydroxyphthalic acid. Isolated from rabbit urine were fifteen metabolites, twelve of which were identified:

1. α - (N-phthaloyliso)-glutamine
2. α - (N-phthaloyl)-glutamine
3. α - (N-phthaloyl)-glutamic acid
4. α - (o-carboxybenzoyl) amino-glutarmide
5. α - (o-carboxybenzoyl) isoglutamine
6. α - (o-carboxybenzoyl) glutamine
7. α - (o-carboxybenzoyl) glutamic acid
8. α - amino glutarimide
9. Phthalic acid
10. Glutamine
11. Isoglutamine
12. Glutamic acid.

Also isolated were three other crystalline unidentified substances which were shown by infrared spectra to be hydroxylated.[11]

The identified twelve compounds were all simple hydrolysis products of thalidomide. Counting both D and L forms of thalidomide over 100 such products are theoretically possible. The presence of hydrolysis products in urine indicated the instability of thalidomide at physiologic pH levels. To confirm the above results, experiments were performed *in vitro* in which thalidomide was incubated at 37° C at a pH of 7.4 in phosphate buffer and was found to gradually decompose (8 percent in 1 hour; 80 percent in 24 hours) forming all twelve known hydrolytic products. Thalidomide was found to be stable within pH ranges of 2 - 6; however, above a pH of 6.5 it decomposed spontaneously. The amounts of each hydrolytic product varied as to the pH encountered.[11] The above information has been confirmed by other workers.[2, 12]

TERATOGENICITY

Workers now turned to the task of determining: (1) The metabolite(s) responsible for the teratogenic effects and (2) The precise mechanism by which the adverse effects were accomplished.

Since the structure of thalidomide differs markedly from the structures of other known sedatives and hyponotics, one may assume that thalidomide metabolism also differs from that of the known compounds. After absorption, thalidomide metabolites are relatively quickly excreted in the urine. In the dog the metabolites are hydrolysis products and consist chiefly of glutamic acid derivatives (as described above). These metabolites of glutamic acid derivation are unique to thalidomide and are suspected to be the causative agents of thalidomide-induced congenital defects.[2, 13, 14] Although active at a cellular level,[15] thalidomide and its metabo-

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A 1968 graduate of the University of Mississippi Medical Center, Gerald M. Robertson, MD, is now taking a psychiatry residency at Central State Hospital in Norman, Oklahoma.

lites were not thought to cause chromosomal abnormalities.[16, 17]

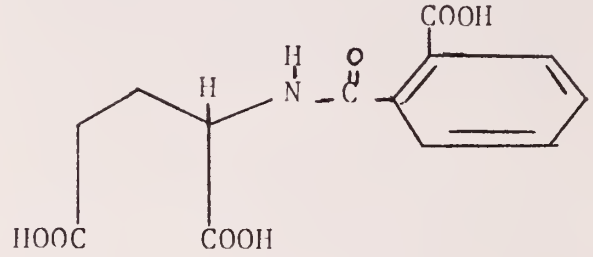
As is already well established, glutamic acid plays several essential metabolic roles: (1) An important protein component, (2) a metabolic intermediate (α-ketoglutaric acid) of the citric acid (Kreb's) cycle, and (3) an amino group donar during transamination processes. Glutamic acid is also active in nervous tissue, for it is a precursor of γ-aminobutyric acid. Glutamine, too, is physiologically important in that it is in equilibrium with glutamic acid and is concerned with the synthesis of urea.

Several metabolites were tested for their inhibitory effects on enzyme systems concerned with glutamic acid metabolism. The three enzymes studied were glutamine synthetase, glutamate decarboxylase, and glutamate dehydrogenase of rat brain. Only the tricarboxylic acid, α-(o-carboxybenzoyl) glutamic acid, was found to inhibit all three enzymes.[18] R. T. Williams obtained approximately the same results in another study.[11] Boylen, Horne, and Johnson report gross abnormalities produced in chick embryos by injecting thalidomide and its hydrolated derivatives into the yolk sac immediately before incubation. Some of the deformity-producing metabolites were found to be derivatives of glutamine.[13]

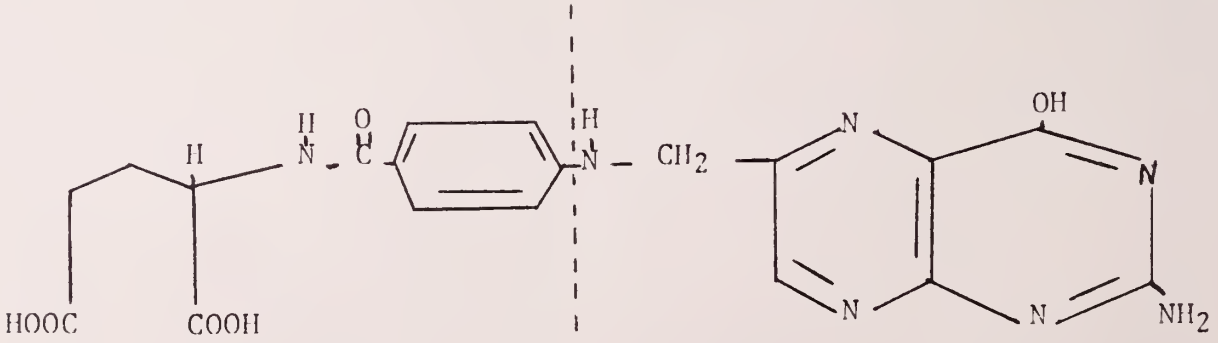
Since glutamine is necessary for purine biosynthesis, interference with nucleic acid metabolism, which occurs very rapidly in the embryo, is a good possibility by which to explain congenital defects. A competitive inhibition is indicated because additional amounts of glutamine protected the embryo against teratogenic effects.[13]

Glutamic acid antagonism is another likely basis for thalidomide's teratogenic effects, for its action resembles that of known glutamic acid anti-metabolites DON (6-diazo-5-oxo-L-norleucine) and azaserine (o-diazoacetyl-L-serine). The two above mentioned compounds are known teratogenics.[19, 20]

It has also been suggested that thalidomide may act as a folic acid antagonist.[2]



α-(o-carboxybenzoyl) glutamic acid



Folic acid

Figure 3

The structure of folic acid certainly resembles the structure of some of the thalidomide metabolites. (See Fig. 3).

It is known that folic acid antagonists are teratogenic in less than lethal quantities.

Thalidomide may also antagonize other B-group vitamins, particularly riboflavin. Robertson treated male patients with thalidomide and encountered increasing allergic reactions along with an occasional case of jaundice and glossitis. The symptoms resembled vitamin B deficiency. A Vitamin B complex was administered prophylactically and the adverse effects were controlled.[21] In animal experiments thalidomide-fed rats demonstrated the same malformations as riboflavin-deprived rats.[22]

Another possible explanation of thalidomide's teratogenicity was that it held immuno-suppressive properties, allowing abnormal pregnancies to be carried to term.[1] Human leucocyte formation (*in vitro*) was appreciably inhibited by thalidomide at concentrations as low as 0.3mcgm/ml. Both D and L isomers demonstrated approximately the same activity as to inhibition of blast formation. The metabolites of thalidomide were also checked as to their capacity for blast inhibition. α - (o-carboxybenzoyl) glutamine and α - (o-carboxybenzoyl) isoglutamine significantly reduced blast formation.[14]

In summary, the exact role of thalidomide's teratogenicity has yet to be thoroughly explained despite several attractive theories.

CONSEQUENCES

An often neglected aspect of the thalidomide controversy are the human results and consequences of only a few months of public use. Where are these children and what can be done for them?

Approximately 520 families over the United Kingdom have a child born with deformities attributed to thalidomide. There are European countries, especially Germany, with as many or more. The functional use of phocomelic upper limbs seemed remote at first and prostheses were used. Mme. Monica Gilbert and Therese Gouin-Decarie in the psychology department at the University of Montreal are eliciting some interesting findings among 76 surviving thalidomide-deformed Canadian children. Some of these children have become as adept with their upper appendages as with their prostheses; the wearing of which seem to decrease, rather than increase, the children's independence. Even at age four, some children believe their arms will eventually grow, while others think their real arms are hidden to be revealed later. Myths surrounding the higher IQ's of thalidomide-deformed children have been refuted by testing. In general, the Montreal group want to protect the children from accepting themselves as freaks.[23]

LIABILITY

Many lawsuits have evolved against firms manufacturing thalidomide. In Great Britain, "Writs were issued against the defendants and the actions were compromised, in terms approved by the court, under which all allegations of negligence against the defendants were withdrawn and the defendants undertook to pay 40 percent of the damages agreed or decided by the court."[24] "Damages totaling $1,045,267 were awarded to 28 British children with deformities allegedly caused by thalidomide. The damages were agreed on by the children's parents and the drug distributor, Distillers Co. (Biochemicals) Ltd. Damages now have been awarded to 49 British children; 11 cases still are pending."[25] Other countries solved their own suits in other ways.

VINDICATION?

Seemingly, efforts to vindicate thalidomide began in about 1965. It was tried on patients with malignancies to no avail.[1]

Sheskin initially reported promising reports on the use of thalidomide in leprosy.[26] After other promising reports,[27] he later found thalidomide to be unsatisfactory as a specific treatment for leprosy. In a study of 24 patients, all having various forms of leprosy, the disease ultimately became worse in 11, and in eight patients there was no change. In five patients improvement was acquired in cutaneous lesions. Side effects which were noticed included: constipation, drowsiness, dryness of mucous membranes, and peripheral edema.[28]

The hypothesis that thalidomide's teratogenicity lay in the fact that it allowed abnormal pregnancies to be carried to term, led to the investigation of the drug as an immuno-suppressive agent.

Roath, Elves, and Israels, as already mentioned, showed that thalidomide inhibited blast formation.[14] Hellman, Duke, and Tucker showed that skin graft survival time was prolonged in mice.[29] This fact, in addition to decreased local lymph node response[30] as well as the effect of the drug on the graft versus host reaction,[31] lent credibility to the immuno-suppressive explanation. Objections to these findings have been raised by other investigators.[32-35]

Habitual thalidomide users for several months have been shown to develop a peripheral neuropathy with sensory symptoms predominating. Weakness was usually mild, involving the proximal rather than the distal musculature. Of 22 patients followed for four to six years after stopping the drug, signs and symptoms were unchanged in approximately 50 percent, improved somewhat in about 25 percent, and disappeared in the other 25 percent. Action potentials of sensory nerves were closely related to the clinical state. Sural nerve biopsies on six patients showed selective loss of large diameter fibers. No demyelinazation was noted.[36]

BENEFITS

Has any lasting benefit come from the thalidomide disaster? Legislation strengthening drug control was passed in this country as well as the tightening of the regulations regarding new drug investigations. It is now a requirement that preliminary tests be run on pregnant animals before a new drug can be given to women of childbearing age.[1]

Research in teratology has been massively stimulated. Perhaps thalidomide will be vindicated by its stimulation of research and thus contribution to scientific knowledge.

In closing, as Frances O. Kelsey states: "One of the more disappointing aspects of the thalidomide aftermath has been that despite rather concentrated research very little definite information as to the mechanism of the teratogenic activity of thalidomide has been gained."[1] □

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Peritoneal Dialysis in the Community Hospital

MELVIN L. BRILL, MD

A relatively simple and inexpensive procedure which can temporarily preserve the life of a patient until a definitive and often reversible lesion can be diagnosed and treated.

THE PURPOSE of this paper on peritoneal dialysis primarily is to sell this procedure to those who have had no experience with it. We know that not many community hospitals have the manpower, time or financial resources to establish hemodialysis units for those relatively infrequent times they are needed. Any hospital, however, can do peritoneal dialysis with a minimum of expense, time and training.

It is generally agreed that, with only rare exceptions, peritoneal dialysis can do everything that hemodialysis can do. In those instances where it cannot, it will at least provide time so that a patient can be moved to a center for hemodialysis.

Peritoneal dialysis is principally used for:

(1) Removal of toxins.
(2) Severe electrolyte imbalance.
(3) Salt and water imbalance; *i.e.*, intractable congestive heart failure.
(4) Acute renal failure or, when the diagnosis is not established, to give time to make a diagnosis.
(5) Chronic dialysis.

PROCEDURE

It has been our experience that most house staff physicians can be shown the procedure once or twice, and then, with the commercially available fluids and stylet catheters, they are able to do them on their own. The routine paracentesis trochar also can be used.

A few features of the procedure bear repetition and emphasis:

(1) Compulsively aseptic technique must be used. This after all is a surgical procedure.
(2) Five to 10 mg. of IV "Valium" is generally enough to settle down even a uremic, combative patient for the procedure.
(3) If necessary, the patient should be catheterized to insure that the bladder is completely empty.
(4) The stylet is inserted approximately two to three inches below the umbilicus in the mid-line, avoiding the larger vessels. Two sensations of "give" will be encountered as the linea alba and then the peritoneum are punctured.
(5) The catheter should then be positioned in the right or left gutter.
(6) If the abdomen is scarred from old surgical procedures, a surgeon can be

asked to do a peritoneal cutdown and place the catheter. Areas of scars should be avoided since the intestines may be adherent to the scar area.

(7) Some people recommend administering two liters of fluid through a spinal needle to expand the peritoneum. I have not found this to be necessary or even desirable, since this may result in extravasation and dissection of the fluid between the abdominal wall and peritoneum, making the procedure extremely difficult.

(8) The fluid should be warmed to 37° centigrade before use, both for comfort and to increase the efficiency of the dialysis.

(9) A meticulous dialysis record should be kept, including medications added to fluids, character of fluid return and fluid balance.

From this point on, the dialysis is conducted entirely by nurses.

DIALYSATE FLUIDS AND ADMINISTRATION

Again let me emphasize that the dialysate fluid should be warmed since this will increase its efficiency.

(1) There are two basic fluids: One containing 1.5 percent dextrose (or 1,500 mg per 100 cc) which is slightly hypertonic; and one containing seven percent dextrose which is markedly hypertonic. Both will result in negative fluid balance. The 1.5 percent solution can remove as much as 300 cc of body fluid per hour; and the seven percent solution can remove as much as one liter of fluid per hour. Since two bottles are usually given at one time, use of one bottle with 1.5 percent dextrose and one with seven percent (4.25 percent solution) produces often desirable, intermediate results.

(2) There is generally no potassium in commercially prepared dialysate fluids and one must be careful to add potassium, especially in digitalized patients. It is well known that potassium dialyzes well, and digitalis dialyzes poorly; hence a great deal of difficulty may be encountered with potassium-free fluids in digitalized patients.

(3) It also may be necessary to add extra calcium to the dialysate fluid if the patient is uremic, acidotic and has a low serum calcium. The correction of acidosis will decrease the amount of ionized calcium and may result in seizures unless extra calcium is given.

(4) Heparin is used in the amount of 1,000 units in each exchange until the fluid returns blood free.

(5) At this point a word about the addition of antibiotics to the dialysate fluid is in order. This is felt to be unwise. The addition of 50 to 100 mg. of tetracycline to each exchange can result in a dangerous accumulation of tetracycline which will greatly accelerate tissue catabolism as evidenced by the rapid rise in blood urea nitrogen levels. It has also been shown that if one does get infection, it is resistant to the antibiotic being added. The best system seems to be to culture the dialysate fluid frequently and treat infection in the standard way.

How these fluids are handled depends entirely on what one is trying to accomplish; whether it be removal of potassium, sodium, water, toxins or the toxic products of uremia.

VOLUME AND RATE OF DIALYSATE ADMINISTRATION

We know that the peritoneum has an area approximately that of the glomerular capillaries, or the twin coil artificial kidney, and it behaves as an inert, semipermeable membrane.

The concentration gradient between extracellular fluid and the dialysate determines how rapidly a substance will diffuse. The larger the dialysate volume, the longer the gradient is maintained, and to a point, the faster the fluid is exchanged, the higher the concentration gradient may be maintained.

Certain practical considerations, however, enter into the decision of how much and how fast to flow the dialysate fluid. More than two liters may compromise ventilation and prove to be unbearably uncomfortable for the patient. Very rapid flows are wasteful

of dialysate fluid and hence very expensive for the patient.

Fifteen millileters per minute urea clearance can be obtained at one liter per hour dialysate flow. Twenty-seven millileters per minute urea clearance can be obtained at three liters per hour flow. A compromise, therefore, of 2.5 liters per hour equals two liters per 48 minutes, which breaks down as follows: ten minutes inflow time, 13 minutes dwell time in the abdomen, and 25 minutes out-flow time. We have been using a ten minute in-flow time, 20 minute dwell-time and 30 minute out-flow time, which works out to one hour per exchange, a round number which is easy for everyone to remember for purposes of calculation.

At this point a word on fluid retrieval is in order. If we have difficulty retrieving the total amount of fluid we have infused during the first few dialyses, we generally go ahead. A positive balance of one or two liters does not delay subsequent exchanges. If, however, consistent positive balance is encountered, flushing the catheter with heparinized saline, repositioning it or even re-insertion may be necessary. It is also important not to let the bottle empty completely or an air lock may ensue.

COMPLICATIONS

Some complications, such as failure to retrieve fluid and peritonitis, have been covered. With respect to peritonitis, my own experience is far below the five to ten percent which one finds reported in the literature. It is usually a staphylococcus or a gram negative organism and these are treated in a standard fashion. It is suggested by some that to reduce the risk of peritonitis, dialysis times be kept under 36 hours.

We have dialyzed as long as three weeks and at post mortem examination, the peritoneal cavity was found to be clean and free of infection.

Another complication we have touched on briefly is abdominal pain and/or compromise of respiration. Occasionally this will require reducing the dialysate volume to one liter.

Bleeding or leakage around cannula sites may require additional suturing, but major bleeding should not be a problem if the puncture is in the mid-line in correct position.

Perforation of the bladder has been reported, but making sure that the bladder is empty at the beginning of this procedure should avoid this complication.

Perforation of bowel with the initial procedure occasionally occurs, and will be announced by the advent of massive diarrhea and/or fecal smelling dialysate. This complication should be rare if patients with significant previous surgery are left for the surgeon to place the cannula. Occasionally late perforation, secondary to pressure of the cannula against edematous bowel, is also seen. This is also more likely with previous surgery and adherent bowel. This complication requires immediate surgery, but dialysis may be continued postoperatively without undue risk.

Loss or inadvertent removal of the cannula can occur. Fixing the cannula to the abdominal wall with sutures and to the dressings with adhesive tape may obviate this possibility. We have made a practice of completely burying the cannula in secure dressings to keep a confused, semicomatose patient from pulling it out.

Severe hypernatremia may occasionally be a problem especially when using hypertonic solutions. Glucose is absorbed, which increases the osmolality of the blood. Water then leaves the cells, entering the vascular compartment which serves to decrease the osmolality. This results in low sodium in the vascular compartment, which is increased by sodium from the dialysate fluid. As the glucose is metabolized and water leaves the vascular space to return to the dehydrated cell, a high concentration of sodium is left behind.

Others feel that the hypernatremia seen is the result of greater water removal than sodium removal and is not dependent on

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hyperglycemia or diffusion of dialysate sodium to extracellular fluid. Regardless of the mechanism, hypernatremia does occur and requires close monitoring of serum electrolyte concentrations.

Protein losses may be very high in peritoneal dialysis with as much as 0.2 to 0.8 grams of protein lost per liter of dialysis fluid removed. This can be significant, especially if one is dialyzing a postoperative renal failure patient who is in negative nitrogen balance and healing poorly due to uremia. In this instance, hemodialysis is preferred.

Hyperosmolar coma has been seen in diabetics when hypertonic solutions are used. This can cause shock and death. We rarely use two bottles of seven percent dialysate solution in one exchange in anyone. A uremic patient has no route to get rid of excess sugar because of his oliguria and in addition is glucose intolerant even if not frankly diabetic.

Lactic acidosis has occurred in people with hepatic insufficiency secondary to failure to metabolize lactose in the commercial dialysate fluid.

ADVANTAGES OF PERITONEAL VERSUS HEMODIALYSIS

(1) Simplicity.
(2) Time—the procedure is underway in minutes.
(3) Psychologically easier to discontinue in a hopeless situation.
(4) Slightly less morbidity and mortality.

DISADVANTAGES

(1) Dialysis efficiency is one-fourth that of hemodialysis and thus takes more time to accomplish the same ends.
(2) It is relatively contraindicated in a hypercatabolic state.
(3) It is risky in a patient with abdominal adhesions.
(4) It cannot be used in patients with abdominal drainage.

SUMMARY

Peritoneal dialysis represents a means of salvage for a significant number of patients who, for a variety of reasons, cannot obtain hemodialysis when a dialytic procedure is needed. It is strongly recommended for community hospitals where hemodialysis is impractical. □

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Special note—Oral contraceptives have been marketed in the United States since 1960. Reported pregnancy rates vary from product to product. The effectiveness of the sequential products appears to be somewhat lower than that of the combination products. Both types provide almost completely effective contraception.

An increased risk of thromboembolic disease associated with the use of hormonal contraceptives has now been shown in studies conducted in both Great Britain and the United States. Other risks, such as those of elevated blood pressure, liver disease and reduced tolerance to carbohydrates, have not been quantitated with precision.

Long-term administration of both natural and synthetic estrogens in subprimate animal species in multiples of the human dose increases the frequency of some animal carcinomas. These data cannot be transposed directly to man. The possible carcinogenicity due to the estrogens can be neither affirmed nor refuted at this time. Close clinical surveillance of all women taking oral contraceptives must be continued.

Indication—Ovulen and Demulen are indicated for oral contraception.

Contraindications—Patients with thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia and undiagnosed abnormal genital bleeding.

Warnings—The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis). Should any of these occur or be suspected the drug should be discontinued immediately.

Retrospective studies of morbidity and mortality conducted in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis, pulmonary embolism, and cerebral thrombosis and embolism and the use of oral contraceptives. There have been three principal studies in Britain[1-3] leading to this conclusion, and one[4] in this country. The estimate of the relative risk of thromboembolism in the study by Vessey and Doll[3] was about sevenfold, while Sartwell and associates[4] in the United States found a relative risk of 4.4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as nonusers. The American study also indicated that the risk did not persist after discontinuation of administration and that it was not enhanced by long-continued administration. The American study was not designed to evaluate a difference between products. However, the study suggested that there might be an increased risk of thromboembolic disease in users of sequential products. This risk cannot be quantitated, and further studies to confirm this finding are desirable.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions medication should be withdrawn.

Since the safety of Ovulen and Demulen in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period.

A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant cannot be determined at this time.

Precautions—The pretreatment and periodic physical examinations should include special reference to the breasts and pelvic organs, including a Papanicolaou smear since estrogens have been known to produce tumors, some of them malignant, in five species of subprimate animals. Endocrine and possibly liver function tests may be affected by treatment with Ovulen or Demulen. Therefore, if such tests are abnormal in a patient taking Ovulen or Demulen, it is recommended that they be repeated after the drug has been withdrawn for two months. Under the influence of progestogen-estrogen preparations preexisting uterine fibromyomas may increase in size. Because these agents may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. In breakthrough bleeding, and in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginam adequate diagnostic measures are indicated. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. Any possible influence of prolonged Ovulen or Demulen therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Ovulen or Demulen therapy. The age of the patient constitutes no absolute limiting factor, although treatment with Ovulen or Demulen may mask the onset of the climacteric. The pathologist should be advised of Ovulen or Demulen therapy when relevant specimens are submitted. Susceptible women may experience an increase in blood pressure following administration of contraceptive steroids.

Adverse reactions observed in patients receiving oral contraceptives—A statistically significant association has been demonstrated between use of oral contraceptives and the following serious adverse reactions: thrombophlebitis, pulmonary embolism and cerebral thrombosis.

Although available evidence is suggestive of an association, such a relationship has been neither confirmed nor refuted for the following serious adverse reactions: neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea during and after treatment, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately post partum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals and mental depression.

Although the following adverse reactions have been reported in users of oral contraceptives, an association has been neither confirmed nor refuted: anovulation post treatment, premenstrual-like syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption and itching.

The following laboratory results may be altered by the use of oral contraceptives: hepatic function: increased sulfobromophthalein retention and other tests; coagulation tests: increase in prothrombin, Factors VII, VIII, IX and X, thyroid function: increase in PBI and butanol extractable protein bound iodine and decrease in T^3 uptake values; metyrapone test and pregnanediol determination.

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Where "The Pill" Began

Selection of Recipients and Donors for Renal Transplantation

MICHAEL H. WHALEN, MD

Criteria for matching kidney transplant partners involve studies of systemic, immunologic and psychologic conditions; some of the major features are presented and discussed.

RENAL TRANSPLANTATION is an acceptable and preferred alternative for the management of terminal chronic renal failure. The recipient of a functioning kidney graft often is able to return to normal activity with a minimum of continuing care. The patient's feeling of mental and physical well-being also is superior to that of the patient on hemodialysis.

The potential benefit from renal transplantation is great but the risks for the recipient remain high. The preoperative preparation, surgical procedure and immediate postoperative management of patients undergoing transplantation require prolonged and intensive medical attention. The patient is subjected to the combined physical stresses of the primary illness, nephrectomy, hemodialysis, transplantation and immunosuppression. For this reason the participants in the transplantation program at the University of Oklahoma are carefully selected. The purpose of this presentation is to list and briefly discuss the guidelines used for selection of transplant recipients and donors at the University of Oklahoma.

The limits of disease and age which preclude a transplantation are not firmly established. Because of this, arbitrary guidelines have been adopted for selection of the ideal transplant candidate. Patients under consideration for transplantation must conform as closely as possible to this ideal. Selection criteria, however, are only guidelines; each patient is considered individually. Some medical problems which prohibit early transplantation may be controlled so that the patient risk becomes acceptable. Renal transplantation is offered only to those patients with primary renal failure as the result of renal parenchymal disease. This includes patients with chronic glomerulonephritis, chronic pyelonephritis, polycystic kidney disease, traumatic loss of the kidneys, malignant hypertension, drug-induced nephritis, cortical necrosis, medullary cystic disease and a number of illnesses which occur infrequently.

Patients with systemic illnesses which have led to renal failure, such as amyloidosis, diabetes mellitus, cystinosis, periarteritis nodosa, and lupus erythematosis are considered poor candidates for transplantation. It is anticipated that the underlying disorder will affect other organ systems and cause recurrent disease in the transplanted kidney. Patients with coronary artery disease and diffuse vascular disease are considered poor candidates for transplantation. Coronary artery disease increases the susceptibility to

myocardial infarction, arrhythmias and complications of fluid and electrolyte imbalance during the stressful operative and postoperative periods. Patients with large vessel atherosclerosis pose operative problems in obtaining an adequate vascular anastomosis. They also have an increased incidence of postoperative intra-arterial thrombosis. Most patients with diabetes mellitus are poor transplantation risks. They are vulnerable to vascular disease and infections and pose major problems in management of the diabetes.

Chemical suppression of normal immunity is a necessity to achieve a successful allogenic renal transplantation. Immunosuppression, however, has several undesirable side effects. Patients with a past history of peptic ulcer disease, tuberculosis, fungal infections and malignancies are considered poor transplantation candidates. Peptic ulcer disease frequently exacerbates under the combined influences of operative and postoperative stress and corticosteroid therapy. Recurrent ulceration, often complicated by bleeding, is difficult to manage and can be lethal. Prophylactic gastric resection has been advocated but has not been our practice. Tuberculosis, systemic fungal infections and malignancies appear to be controlled by the same lymphocyte-mediated immune mechanisms which must be suppressed to allow a successful transplant. As a result, these diseases frequently exacerbate during immunosuppressive therapy. Recurrence of tuberculosis can be prevented with prophylactic therapy; similar prophylactic antifungal therapy is not justified because of the potential toxicity of antifungal drugs. Patients with malignancies may develop an accelerated course during immunosuppressive therapy.

Each patient is carefully evaluated for anatomic defects of the lower urinary tract. Whenever possible, these defects are corrected. If an adequate correction cannot be accomplished, the patient is not considered for transplantation. The transplanted patient with uncorrected lower urinary tract obstruction is likely to develop urinary tract infections which threaten survival of the graft.

Our patients are examined by a psychiatrist and clinical psychologist. The purpose is to exclude patients who are psychotic or who have disabling character disorders. The relationship between patient, physician and staff is very close and prolonged when transplantation is undertaken. A successful transplant is more likely if the patient is able to cooperate, follow instructions and adjust to the necessary dependency upon the physician during the course of the illness. Psychotic individuals and persons with a past history of severe depression or self-destructive tendencies are less able to enter into a mutually dependent and cooperative relationship and are, therefore, at high risk.

SELECTION OF DONOR

The ethical and legal aspects of organ donation will not be considered in this presentation. The discussion will be confined to the medical criteria for donor selection.

The two major sources of kidneys for transplantation are living related donors and unrelated cadaver donors. To obtain maximum graft survival and function, donor organs should be easily transplanted and capable of completely normal function. Therefore, before transplantation, the quality of the organ must be evaluated. The parameters of anatomy and function which are measured are the same for living donor and cadaver donor kidneys. Evaluation of a live related donor is designed to protect the donor as well as to assure a high rate of success for the graft. Donation of a kidney by a living individual with two normal kidneys does not substantially affect the donor's longevity. Donation of an organ that is diseased may reduce the longevity of the donor and almost certainly will function poorly in the recipient. The donation of a cadaver organ usually takes place as an emergency and in circumstances where the preoperative evaluation of the donor patient is impossible. Therefore, the evaluation of the organ is frequently made on the basis of the immediate ante mortum course and after the kidneys are obtained.

The most suitable kidney for transplantation is anatomically simple. This means the kidney should be of normal size and have one artery, vein and ureter. The incidence of

anomalies in the arterial or venous supply or ureteral drainage of the kidney exceeds 25 percent.[1] The anatomy of the kidney from a live donor is determined by preoperative intravenous pyelography and arteriography. The anatomy of the cadaver kidney is evaluated at the time the organs are obtained.

The donor kidney must be free of infection and evidence of intrinsic disease. Several routine urinalyses should be performed to insure that the urine is free of bacteria, protein, cells and casts. Infection or any other abnormality on urinalysis is sufficient to disqualify the live donor. The urinalysis from a cadaver donor must be interpreted in light of the patient's past history and the events, usually traumatic, which have resulted in death.

The ideal kidney will demonstrate normal function. The blood urea nitrogen or serum creatinine, and serum and urine electrolytes of the donor should be normal. A live related donor should have a normal creatinine clearance and equal dye excretion from each kidney on intravenous pyelogram. On occasion inulin and para-aminohippuric acid clearance studies are obtained. Only rarely is it possible to obtain complete renal function tests on a prospective cadaver kidney. A normal urinalysis, blood urea nitrogen and serum creatinine and an adequate volume of concentrated urine is presumptive evidence for normal renal function. It is also possible to assess the function of cadaver organs *in vitro* prior to transplantation by utilizing one of several kidney preservation machines available.

HISTOCOMPATIBILITY TESTING

The final phase of donor and recipient selection is assignment of a donor organ to a recipient. ABO compatibility first must be established. Two tests are then available for matching the HL-A cellular transplantation antigens. These are the microcytotoxicity tests and the mixed lymphocyte culture. Currently, the HL-A transplantation antigens are thought to be cell surface characteristics which are the products of two co-dominate alleles. Each allele contains two gene subloci which in turn control the cell surface antigens. The first sublocus has a minimum of eight alternative antigens. The second sublocus has a minimum of fourteen alternative antigens. The two series of antigens are mutually exclusive. Thus, an individual can be characterized for the major transplantation antigens if four antigens, two from the first sublocus alternatives and two from the second sublocus alternatives, are identified.

Application of this information to the selection of appropriate live related donors has resulted in improved kidney graft function and survival and a reduction in the quantity of immunosuppressive agents required for maintenance of the grafts. The best results are obtained when HL-A identity between a sibling donor and recipient can be established. Good graft function and survival is expected also when a graft is made from parent to child.

The lymphocyte typing data for a live related donor-recipient pair are always interpreted within the context of the lymphocyte typing of the parents and other siblings. This procedure, called haplotype analysis, consists of assigning to hypothetical chromosomes the HL-A specificities found in the parents. Assignment of specificities is based upon an analysis of the typing of the siblings. The hypothetical chromosomes are then traced into the siblings as co-dominant alleles. An optimal donor-recipient pair is genotypically identical for the HL-A antigens as the individual inherits identical chromosomes from both parents.

A second test of HL-A identity is the one way mixed lymphocyte culture proposed by Bach.[2] In this test lymphocytes from donors (one cell line) are mixed with lymphocytes from recipients (other cell lines) and placed in tissue culture. If the donor and recipient are identical for the transplantation antigens, the cells in lymphocyte culture do not proliferate. When the transplantation antigens of the mixed lymphocytes are not identical, proliferation of lymphocytes oc-

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curs. Cellular proliferation is conveniently measured by the uptake of tritiated thymidine placed in the culture seven days after the cells are planted. A response of only one cell line (one way stimulation) is achieved by blocking the stimulating cell line with Mitomycin-C.

The criterion for an acceptable sibling-sibling donor-recipient pair is HL-A identity by haplotype analysis and non-stimulation in reciprocal one way mixed lymphocyte culture.

Kidney donation for up to ten percent of potential recipients might be obtained from live related donors. The remaining transplant recipients must be accommodated with grafts obtained from cadavers. Lymphocyte typing alone is used for the matching of cadaver donor and recipient. Lymphocyte typing of unrelated individuals allows the determination of the HL-A phenotype. In clinical practice we obtain the best possible antigenic match between the donor and recipient. An ideal match is an identical match for four HL-A antigens. The value of antigen matching in unrelated donors is still controversial. The prevailing opinion is that good antigen matching contributes to but is not the sole determinate of good graft function in the recipient of an unrelated cadaver kidney.

Kidney donations occur infrequently. Therefore, an attempt is made to utilize all kidneys donated. This means that less than ideal tissue matches must be accepted for transplantation. The major contraindication to utilization of a kidney is the presence in the recipient's serum of preformed lymphocyte antibody against donor cells. The need to utilize all available organs and to find the best donor-recipient match has prompted the establishment of a cadaver organ exchange network. The University of Oklahoma Medical Center participates in such a multicenter network.

SUMMARY

The criteria by which the prospective kidney transplant recipient and donor kidney are selected at the University Medical Center have been reviewed. A summary of the role of histocompatibility testing in this procedure has also been presented. □

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Hospital vs. Home Hemodialysis

L. O. LAUGHLIN, MD

Home hemodialysis, an effective means of providing care for select patients with chronic renal failure, should have rehabilitation as its goal, as well as immediate care.

SINCE THE first publication describing use of an artificial kidney in the early 20th century by Able and Rountree, physicians have increasingly improved this effective technique for the treatment of renal failure that no longer responds to conservative therapy. One of the problems that prevented earlier extensive utilization of long term, maintenance hemodialysis was the inability to maintain A-V shunts that could be used repeatedly for hemodialysis without clotting complications. In 1960, Scribner and others described the use of teflon cannulas that provided a nonwettable surface for external A-V shunts and resulted in a marked prolongation of shunt life and a more practical approach to repeated dialysis. Since then, additional experience has been obtained with the use of direct arteriovenous anastamosis. By connecting the radial artery and vein, the vein becomes dilated and thickened ("arteriolized") making it easily accessible to multiple venipunctures with large needles allowing high flow rates. By the use of these two shunt methods, hemodialysis units have become rather common in larger hospitals.

With the formation of each new hospital dialysis center, it became apparent there were more patients in need of dialysis than there were units available. Inpatient dialysis increased at rather alarming rates. Kidney transplantation became more practical, especially with back-up dialysis available to patients developing complications and to prepare patients optimally prior to transplant.

Because of the increasing number of patients requiring dialysis, it became quite obvious that means other than inpatient dialysis must be developed. In 1964, Scribner, *et al.* in Seattle reported their experiences with outpatient and home dialysis and described this more practical approach of home training which has proven to be as effective as, if not superior to, inpatient dialysis.

The most obvious advantage of home dialysis is to provide more room in the hospital for acutely ill patients and for the never-ending list of new patients with chronic renal failure. If patients requiring dialysis are not provided alternatives such as transplantation or home dialysis, the capacity of in-hospital dialysis units would become rapidly saturated and no new patients could be accepted. Another important advantage is the reduction in the cost per dialysis to the patient. In-hospital dialysis averages between $150 and $250 per dialysis, depending upon the locale, for the chronic renal failure patient as opposed to the operational cost of $30 to $50 per home dialysis. The third prime consideration for home dialysis is rehabilitation. In most cases an independent patient functions more

effectively than one who leaves responsibilities of his management to others.

The training program for home dialysis should begin with the patient. Only after he feels confident of his ability to operate and understand dialysis should training be extended to his mate or another responsible family member. This method allows preservation of independence and maintenance of identity; both important factors in rehabilitation. The central figure responsible for instructing home dialysis patients is the dialysis nurse who remains in almost constant contact with the patient during the early period of training. We rely on her to relay patient problems or anxieties to us so that appropriate measures can be taken for additional training or reassurance to the patient. Other advantages of home dialysis which should be mentioned, but lack of time prevents discussion, are the decreased incidence of shunt infections or occlusion, hepatitis, and other hospital-endowed infections.

There are those patients in whom home dialysis may fail, such as the prepuberty patient, or the patient who fails to make the necessary psychosocial adjustments. Patient training failure in most instances, however, is the result of inadequate training. The patient with complications of chronic hemodialysis, that is cardiac failure, A-V cannula complications, infection, hemorrhage, metabolic bone problems, pericarditis, etc., will have to return to the inpatient unit until adequate therapy can be provided. Needless to say, the patient with acute renal failure would have to be dialyzed in the hospital.

I should like to review briefly a report from the National Dialysis Registry in regard to dialysis centers and home programs as of February, 1971. There were 303 centers contacted with 88 percent replying. There were a total of 3,528 patients on hemodialysis of which approximately 2,100 were dialyzed on an outpatient hospital program and 1,400 were dialyzed in the home. The average overall age of this group both at home and in the center was about 40 to 42 years. The largest single five year age group requiring hemodialysis consisted of 560 patients between the ages of 45 and 49. There were 21 patients under the age of nine, and 46 patients above the age of 65 receiving maintenance dialysis. This report serves as a rough guideline to the number of hemodialyses that are currently being employed throughout the United States and reflects an increasing utilization of hemodialysis. The experience in Oklahoma is summarized in a recent article by B. J. Matter, MD, in *The Journal of the Oklahoma State Medical Association.*

Briefly, in Oklahoma, dialysis facilities within the hospital now are available in Stillwater, Miami, Pawnee, Bartlesville, as well as in various hospitals in Oklahoma City and Tulsa. In addition, 17 patients are currently being dialyzed at home.

It has been shown, therefore, that when conservative means for the treatment of renal failure fail, an effective, rational approach may be obtained with the use of hemodialysis. Hopefully, we can adopt a program similar to that demonstrated to be effective in Seattle. In this program approximately 60 percent of the dialysis cost is paid by the patient or private insurance carrier; 20 percent of the financial support is obtained from private contributions and only 20 percent is from government sources. Our goal is not merely to prolong the life of the patient, but to promote rehabilitation and, in selected instances, perform kidney transplantations. With the development of dialyzing membranes that are more economical and with improved dialysance of waste material, this goal is being attained. Our concern regarding the expense of such a program even for the home dialysis patient, however, remains justified. □

L. O. Laughlin, MD, graduated from the University of Oklahoma College of Medicine in 1959 where he is now Assistant Clinical Professor. His practice is limited to his specialty of internal medicine and nephrology. Doctor Laughlin is a member of the International Society of Nephrology.

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OSMA JOURNAL/special

Medicine in Southwestern Oklahoma Before Statehood II

Fort Sill, I.T., 1869-1875

DORIS BULLOCK
EVERETT R. RHOADES, MD

One hundred years ago malaria and "typhomalaria" affected almost every person at some time during their stay at Fort Sill. Sanitation procedures such as discontinuation of watering of horses in Medicine Bluff Creek above the source of water for drinking and bathing were associated with amelioration of some of these conditions.

THE ANTECEDENTS of "American"* medical practice in the Indian Territory before statehood of Oklahoma are found only in the few physicians hired by the Bureau of Indian Affairs to care for its Indian wards or physicians assigned to military duty with troops serving in the area. Because of the importance of Fort Sill in the history of this area and the importance of military medicine in the medical history of Oklahoma, this report presents a review of health conditions at this army post. These conditions are those existing one hundred years ago in "Oklahoma," west of the 98th ("Indian") meridian. The period reported coincides with the earliest years of Fort Sill's existence and is of further interest because it marks the close of the Indian wars on the southern plains, and the beginning of a "quiescent" period before opening the area to white settlement.

During this period and even until statehood there was a great disparity between medicine (and most other aspects of daily life) as practiced in the eastern and western territories. By 1874, the "five civilized tribes" had achieved a high degree of civilization with schools, churches and medical practice equivalent to that of the neighboring states. On the other hand, for 50 years after settlement of the five civilized tribes in eastern Oklahoma, the Kiowa and Comanches were still desperately trying to preserve a way of life and freedom in the adjacent western half of the state. The two territories were and are dissimilar topographically, demographically and socially.

During the time before statehood, medical practice, especially along the frontier military outposts, was a continuation of practices used and developed in the war between the states. Medicine was on the threshold of a great renaissance beginning with the development of bacteriology and the discovery of a specific etiology for individual diseases. The discoveries of Koch and Pasteur not only marked the beginning of modern scientific medicine but, as we shall presently see, were of direct consequence to those hardy individuals who found them-

*This term is used to differentiate "American" medicine from "Indian." The latter was practiced in this country with a high degree of skill from antiquity, with results often superior to that of "American" medicine.

Presented in part at the December 8th, 1966 meeting of the History of Medicine Society, Oklahoma City.

selves caring for the sick and wounded at a small army outpost at the far eastern end of the Wichita Mountains in Indian Territory.

MEDICAL CONCEPTS IN THE U.S. DURING THIS PERIOD

Diseases had to do in a very prominent way with *fevers* as nosological entities and the clinical descriptions of syndromes of fevers. Thus, there was the yellow fever as contrasted to other fevers. There were *the* intermittent fevers, sometimes shortened to the "intermittents," often regarded as "malarial" but obviously by no means always malarial. At this time "fevers" rather than representing *symptoms* of disease were regarded as *diseases*. Thus fever as "final diagnosis" might be called "typhoidal," "intermittent," "recurrent" or "malarial" (sometimes "tertian," "quartan," "malignant quartan") to distinguish them from "yellow" or "spotted" or "enteric" fever. Sometimes it was difficult to distinguish between fevers clinically in which case they might be called, for example, "typhomalarial" a diagnosis made with some frequency at old Fort Sill. Benjamin Rush, the first great American physician, thought there was only one "fever," caused by *debility* which led to *irritability*, an idea arising from his study of Cullen[1] and Brown.[2] This led naturally to the form of therapy espoused by Rush: reduction of excitability of blood vessels (basically by bleeding), low diet and purging.[3]

The classic work by Wunderlich[4] on clinical thermometry surely was not yet recognized widely by the time described in this paper. The cause of fever, in contrast to the situation today, was almost invariably an infection.

Pneumonia of course could be diagnosed with the stethoscope and "consumption" could be diagnosed clinically in its late stages. Certain diseases of the heart were distinguished, such as "inflammation of the endocardium" (probably endocarditis) and "valvular disease of the heart." The latter condition was almost surely rheumatic in the great majority of instances. Surgical diseases included hernia, varicocele, (surprisingly, mentioned rather often) and buboes. In an army post, of course, wounds were an important item. One would expect a majority of wounds to be caused by arrows but by the 1870's the Indians had enough firearms that arrow wounds were less common. In spite of the horrors of Indian savagery, wounds, including fatal ones, at Fort Sill more often than not were inflicted by the soldiers' "friends."

FORT SILL 1870-1875[5]

Until the awful winter* of 1874-1875, garrison duty at Fort Sill was not too remarkable. There were mild skirmishes with hostiles but the forbearing and permissive attitude of the liberal Quakers charged with the care of the Indians prevented punitive military measures. Finally, when the raiding of the Indians became intolerable, control of the tribes was transferred to the Department of the Army July 26th, 1874.[6] This transfer loosened the restraints on the army and led to the intensely bitter campaign of the winter of 1874-1875. It is no accident that so many of the successful army campaigns occurred in the midst of winter,** and this year was no exception. Conquering of Indians always depended upon destruction of lodges, food stores and horses. During this period Fort Sill was under the command of Col. (Brevet Maj. Gen.) John "Blackjack" Davidson, a skilled and relentless Indian fighter whose fame has been overshadowed by that of MacKenzie and Custer, both of whom had short tours of duty at Fort Sill.

MEDICAL OFFICERS

During this time there were three classes of medical officers at Fort Sill: Surgeons (rank of Major); Assistant Surgeons (Captain or Lieutenant) and Acting Assistant Surgeons (civilian contract physicians). The surgeon, in addition to holding sick call and carrying out hospital duties, acted in a much broader capacity, keeping the mean

*The fall of 1874 was called the "wrinkled-hand winter" by Kiowas because of the unusual amount of cold rain and the constant pursuit by the soldiers which prevented drying of the skin of the hands.

**For example, Custer at the battle of the Washita.

Table 1
FORT SILL SURGEONS, 1869-1875

Collins, Joseph H.	A.A.S.	March '69-July '69
Forwood, William H.	Asst. Surgeon	July '69-May '70
McKay, R. H.	A.A.S.	Jan. '70-Sept. '71
Wise, J. H. P.	A.A.S.	June '70-July '70
Brown, J. M.	Asst. Surgeon	Dec. '70-May '74
Snively, D. S.	A.A.S.	March '71-April '71
Arms, C. C.	A.A.S.	July '71-Oct. '71
Gessin, B.	A.A.S.	Sept. '71-April '72
Gessin, B.	A.A.S	Sept. '72-Dec. '72
Cleary, F. T.	A.A.S	Dec. '72-Oct. '73
Newell, J. M.	A.A.S.	July '73-Feb. '74 & July '74-Aug. '74
Knight, C. W.	A.A.S.	Dec. '73-Jan. '74 & Mar. '74-Dec. '74
Town, F. L.	Surgeon	May '74-May '78
Hatch, G. W.	A.A.S.	July '74-March '75
Barnett, R.	A.A.S.	Oct. '74-Dec. '74
Grinnel, F.	A.A.S.	Dec. '74-April '75
Smart, D. S.	A.A.S.	Mar. '75-April '75
Allen, S. J., Jr.	A.A.S.	May '75-Aug. '75

strength of command, making daily weather observations, conducting monthly sanitary inspections, noting the character of cooking and quality of rations, inspecting clothing, recording births and deaths, and observing health conditions on the post, particularly the source of drinking water.

A list of medical officers is given in Table 1. For the first five years, Fort Sill had no physician with the rank of Surgeon. The first to hold that rank was Francis L. Town, who served at Fort Sill from May 29th, 1874 to May 21st, 1878. His entries in the Medical History reflect a high degree of intellect and thoroughness. The first physician was Acting Assistant Surgeon Joseph H. Collins (March to June, 1869).

CONDITIONS IN THE FIELD

An example of the kind of activities that the soldiers were called upon to carry out and the duties associated with being an army surgeon is found in the monthly report for August of 1873,[7] in which an expedition consisting of companies G, H, K and M of the 10th Cavalry and Company C of the 11th Infantry, under the command of Lt. Col. Davidson accompanied by Assistant Surgeon Brown and Assistant Army Surgeon Newell and Hospital Steward Underwood left the post on August 19th on a scouting party. This party returned in September, 1873 "on the 14th instant having been gone 27 days and made a march of about 400 miles."[7] During the winter of 1873-74 there were many such scouting parties usually accompanied by physicians.

In 1874 the most intense Indian fighting took place from Fort Sill and coincided with the winter in which the Indians were finally subdued. In the fall of '74 the soldiers finally chased the Indians onto the staked plains and into Palo Duro Canyon with destruction of virtually all of the Indians' supplies and horses. The wet winter of this fall has already been alluded to. The surgeon's reports often gave interesting accounts of military actions. A typical encounter with the Indians was noted by the Post Surgeon in August of 1874: "On the morning of August 21st a command left for Wichita

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Agency arrived about 12:00 midnight on the 22nd—an attempt was made to compel Red Food's band of Comanches to surrender and return to Fort Sill. A fight ensued—the Comanche Camp was burned—three soldiers wounded. On the 23rd some further scrimmaging ensued—one soldier wounded. On 28th Company C and H returned to Fort Sill."[7]

In September the ratio of sick to mean strength of 1,000 jumped to 235. Nearly 24 percent of the troops were ill at this time! The long cold marches must have been most tedious for the surgeons attending the troops. A notation in September, 1874 mentioned that "an expedition against hostile Kiowas, Comanches commanded by Lt. Col. J. W. Davidson, 10th Cavalry, Medical Officer Surgeon F. L. Town, U.S.A." left Fort Sill I.T. September 10th and moved "north to Washita River—thence to the west up this river some 50 miles and passing yet westward crossed north fork about 100 degrees, 30 minutes west longitude—no Indians have been met with. Distance marched 298 miles." A picture of health conditions in the field is starkly painted by the entries in the surgeon's reports of soldiers transferred to the hospital from columns in the field. For example in Table 2 is shown such a report for the month of October 1874. A variety of maladies are present including items such as "tumor," old gunshot wound, inguinal hernia, conjunctivitis, phimosis, varicocele and acute diarrhea. Further hardships were encountered in November when eleven men were transferred to the post from the field for frostbite, and in the same month troops encountered the scene of a battle with the Cheyennes against Captain Townsend, on the banks of the north fork of Red River, where "was found 1 dead, mutilated and scalped." This man was buried on November 11th during a violent northern rain and sleet storm.[7]

Table 2
FORT SILL—OCTOBER, 1874

The following men were transferred to Post from Fort Sill column in field:

Sgt. Charles Fairalds	Tumor
Pvt. Robert Jackson	Varicocele
Pvt. William Humans	Old gunshot wound
Pvt. Benjamin Griffan	Varicocele
Pvt. James Williams	Old contusion
Pvt. Aaron Myloro	Contusion left leg
Pvt. James Lane	Abscess
Pvt. Simon Turnor	Phimosis
Pvt. Benjamin Brown	Inguinal hernia
Pvt. Charles Hicks	Tertian intermitt. fever
Pvt. John Glasgow	Conjunctivitis
Pvt. James Erwin	Gunshot wound rt. forearm
Pvt. John Shea	Valvular disease heart
Pvt. Robert Johnston	Inguinal hernia
2nd Lt. Patrick Kellicker	Varicocele
	Acute diarrhea

CONDITION OF THE INDIANS

The Indians who were captured and brought into Fort Sill at this time were in particularly pitiful condition because of crowded conditions and inadequate provisions for taking care of the prisoners. In a letter from J. A. McCoy (A.A. Surgeon, USA) to the Post Adjutant, December 12th, 1874:

> Sir, In obedience to the instructions, contained in a letter from headquarters, Fort Sill Indian Territory, on date Dec. 2nd, 1874 I have visited daily and examined the ice house, used as a prison for 103 Indians and would respectfully recommend construction of a sufficient urinal to carry the urine outside of the building and the application of lime to the ground now saturated with urine. The removal of the tents and a thorough policing of the grounds around the building, and removing of the beast's bones and other decayed debris. A more abundant supply of water and basis (sic)* for personal cleaniness. Health good except two cases of fever, intermittent and one of pneumonia. Very respectfully, J. A. McCoy, A.A. Surgeon, USA.[7]

This was forwarded through F. L. Town, Post Surgeon, who felt that the construction of the urinal for the Indian prisoners in the ice house was very important. "It would appear the vacant ground floor at the end of the prison room is saturated with secretions. A daily supply of water is very insufficient for the number of prisoners. This means of personal cleanliness appeared to be much needed: Signed, F. L. Town, Post Surgeon." These extremely unsanitary and unsatisfactory conditions for living undoubtedly contributed to the high death rate of the Indians during this period of time.** The Indians lived in a condition of frank starvation during this winter.

*probably "basins"

**In the authors' opinion, tuberculosis, not previously known to be common among the Southern Plains Indians probably got its "start" at about this time. It did not become rampant for another 20 years, when it often obliterated entire families.

Table 3

FORT SILL, INDIAN TERRITORY
CONSOLIDATED SICK REPORT (COLORED), FORT SILL, INDIAN TERRITORY
1870-1874

Year	* 1870-71		** 1871-72		*** 1872-73		1873-74	
Mean Strength Enlisted Men	494		506		341		313	
DISEASES	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
GENERAL DISEASES, A								
Typhoid Fever	1	1	—	—	—	—	—	—
Typho-Malarial Fever	—	—	1	3	—	—	—	—
Remittent Fever	1	—	11	—	1	—	1	—
Intermittent Fever	293	—	247	—	113	—	82	—
Other Diseases of This Group	5	—	14	—	53	1	25	—
GENERAL DISEASES, B								
Rheumatism	11	—	49	—	53	1	57	—
Syphilis	10	—	5	—	14	2	9	—
Consumption	—	2	6	1	—	—	—	1
Other Diseases of This Group	8	—	11	—	5	—	7	—
LOCAL DISEASES								
Catarrh and Bronchitis	54	—	229	—	52	—	101	—
Pneumonia	3	3	2	—	—	—	3	—
Pleurisy	1	—	5	—	2	—	3	—
Diarrhea and Dysentery	114	1	141	—	78	—	59	—
Hernia	—	—	2	—	2	—	6	—
Gonorrhea	1	—	1	—	8	—	1	—
Other Local Diseases	46	2	202	1	189	—	162	2
TOTAL DISEASES	548	9	926	5	670	4	516	3
VIOLENT DISEASES AND DEATHS								
Gunshot Wounds	8	3	21	—	6	1	6	1
Drowning	—	2	—	—	—	—	—	—
Other Accidents and Injuries	63	—	125	—	118	—	83	—
Homicide	—	1	—	—	—	—	—	1
TOTAL VIOLENCE	71	6	146	—	124	1	89	2

*six months only
**three months only
***five months only

CONDITIONS AT THE POST

The living conditions of the soldiers were often not a great deal better than for the Indians, except for crowding. Surgeon F. L. Town noted in regard to sanitation that: "Excreta received in the wooden boxes which are removed and emptied frequently. The boxes should be lined with zinc as they now leak, and the soil in the vicinity is filled with the liquid portions. This is probably the most urgently needed sanitary measure at the Post." The report for January, 1875 stated that facilities for hand washing and face washing were woefully inadequate for the troopers and the recommendation was that water basins and towels might be purchased from the company fund. Conditions in the primitive situation of the frontier post often magnified otherwise seemingly unimportant conditions; for example, Assistant Army Surgeon G. W. Hatch was on sick report March 25th for "piles." He was returned to duty on March 27th. The method of therapy is not stated.

On March 22nd, Col. R. S. MacKenzie of the 4th Cavalry assumed command of the post relieving Lt. Col. J. W. Davidson, 5th Cavalry who moved into camp preparatory to marching to Texas. On April 28th, Lt. R. G. Carter was seen at sick call because of varicose veins.*

*Lt. Carter wrote one of the great classics of southern plains Indian wars, "On the Border with MacKenzie."



Figure 1. Post Hospital, Fort Sill. This was the original permanent hospital built at the post. Construction began October, 1871 and was completed the following year. Courtesy Fort Sill Museum. Date of photograph not known.

Providing potable water proved to be a vexing problem. An example of the type of water supply available is given in the report for April, 1875 in a letter to the Post Adjutant at Fort Sill: "In some of the Companies additional vessels are required—also covers for the water barrels are much needed to exclude the dust and sand which is blowing into them." The hospital had a cistern but water for the rest of the post came from the creek. The drainage of water including slops and laundry water was an important item and entries were frequently made regarding the drainage of the post.

Malaria was an important disease during this time and it was noted that on April 24th, a white butcher employed by the Beef Contractor died of quartan intermittent fever with chronic hepatitis.

The Surgeon had the usual difficulty with the command in securing his sanitary requests. For example in May, 1875 he again made the following recommendations: "The recommendations of last month in regard to sheltering the water barrels from the sun and providing covers to exclude the dust are respectfully renewed. As it is conceded to be of very great importance to the health of individuals that the water furnished for drinking and domestic purposes should be preserved as free as possible from organic impurities, it is believed that the camping of troops or Indians above the Post on Medicine Creek which affords the water supply of the garrison is very liable to result in the introduction of various organic matters into the water and influence the health of the command unfavorably. Likewise the watering of public animals, in or near the locality from which water is brought is also likely to result in a certain amount of contamination. Also the watering of large numbers of animals daily above the Post has occasioned the distribution of deposits of fine sediments containing more or less animal matter along the bed of the creek where it flows immedi-

Table 4
FORT SILL, INDIAN TERRITORY
CONSOLIDATED SICK REPORT (WHITE), FORT SILL, INDIAN TERRITORY
1870-1874

Year		* 1870-71		** 1871-72		*** 1872-73		1873-74	
Mean Strength	Officers	19		83		19		16	
	Enlisted Men	101		4		67		47	
DISEASES		Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
GENERAL DISEASES, A									
Typho-Maralial Fever		—	—	1	1	—	—	—	—
Remittent Fever		—	—	—	—	1	—	—	—
Intermittent Fever		139	1	12	—	23	—	29	—
Other Diseases of This Group		—	—	—	—	4	—	3	—
GENERAL DISEASES, B									
Rheumatism		3	—	5	—	8	—	6	—
Syphilis		—	—	—	—	1	—	2	—
Consumption		—	—	2	—	—	—	—	—
Other Diseases of This Group		—	—	—	—	—	—	1	—
LOCAL DISEASES									
Catarrh and Bronchitis		10	—	13	—	11	—	15	—
Pneumonia		1	1	—	—	—	—	—	—
Pleurisy		—	—	2	—	—	—	—	—
Diarrhea and Dysentery		29	—	—	—	8	—	13	—
Hernia		—	—	—	—	—	—	2	—
Other Local Diseases		9	—	6	—	9	—	29	—
TOTAL DISEASE		191	2	41	1	65	—	101	—
VIOLENT DISEASES OR DEATHS									
Gunshot Wounds		1	1	1	—	—	—	1	—
Other Accidents and Injuries		3	—	1	—	4	—	8	—
TOTAL VIOLENCE		4	1	2	—	4	—	9	—

*six months only
**three months only
***five months only

ately by the Post. This sediment is exposed to decomposition as the season advances since the volume of the creek dwindles in mid summer to a feeble current which mostly percolates beneath the gravel. During the past season the bed of the creek was observed in an insanitary condition from this cause and emitted a decidedly unpleasant odor."[7] This is a most emphatic statement of the observation of an association between contamination of drinking water and disease.

An interesting anecdote concerns a dispute between the post surgeon and Gen. Grierson regarding the location of the hospital away from the stables, a view much favored by the surgeon. Grierson noted that the hospital was as near the barracks as the stables and besides "whoever heard that it was unhealthy to be near the stables?"

A further problem of environmental contamination at the Post was a covered drain that had been dug immediately behind the company kitchens on the west side of the garrison. After its construction it was found that the drain invariably became clogged and overflowed and that the decomposition of slops and especially garbage and fragments of meat which the cooks could not be prevented from throwing into the drain, gave rise to "an exceedingly pungent and offensive effluvium" which came up through the gratings. The drain discharged its contents on the slope just beyond the barracks. The emanations were considered likely to be productive of "most mischievous results" and might even originate an epidemic so that the use of the drain was discontinued and the grating securely packed over. "The openings have not since been uncovered until the arrival of the present

command during the past month. After the shower last evening, a distinctly septic odor hung around the post and more particularly about the hospital and grounds which has been traced to this drain, the wind being from that direction."[7]

An inspection of the deaths associated with gunshot wounds clearly indicates that the Indians were not the most hazardous enemy that the soldiers could have. Rather, more individuals were shot and killed through brawling, often with friends, and by accidental shooting than by the Indians during the years of 1874-1875.

It is of interest that in this relatively small command there was a rather high incidence of suicides, which almost invariably were by shooting. One can only guess what severe mental pressures were placed upon the individuals in this command. It must be remembered that the 10th Cavalry was made up of Negro troopers not yet ten years after the Civil War. The frontier life and dramatic change from their living conditions must have been particularly difficult for the Negroes to adjust to. For example, a note on October, 1875 is as follows: "Pvt. Charles gunshot wounds through the chest died October 22nd, 1875. He deserted October 20th from detached 4th Cavalry enroute from Caddo, Indian Territory to Fort Sill. He was apprehended the same night, the 20th, and is reported to have committed suicide on the morning of the 22nd. His remains were brought to this post and buried the 23rd."

Nevertheless, there were moments of brief pleasure for at least some of the troops, occasionally accounting for some of the illnesses also. For example, General order No. 36, June 15th, 1874 notes "whereas Private _____ was without trousers, coat, hat or shoes and under the bed of one _____ laundress, he was fined $10.00."

A summary of health conditions for the years 1870-1874 is shown in Tables 3 and 4. Because the data for the first three years are for only a few months of each year, conclusions as to prevalence of various diseases should not be made. The mean strength of the garrison in 1873-74 was also only from fifty to sixty percent that of 1870-71. Crowding in barracks was therefore less a problem. For example, the barracks were designed for 388.57 cubic feet per man in a company of 100 but in 1874 the companies contained approximately 60 men with a resultant air space of 647.61 cubic feet. Adequate space per man and adequate ventilation were recognized as important for the health of troops. These tables are of interest because of the insight into types of diagnosis made by the physician. The classification "other local diseases," unfortunately leaves much to the reader's curiosity.

Assistant Surgeons H. S. Kilbourne and J. M. Brown wrote a description of the hygiene of the post,[8] summarizing four years 1870-1874 along with a description of the post. Significant observations by these authors include a note that in the rear of each barracks was a "privy of the earth closet type" located not far from the laundries. They further note that the hospital, designed for a capacity of 24 beds, and although not yet completed, had been partially occupied for over one year. There was no lavatory in barracks or hospital and no bathing facilities were available "had the men been so disposed."

Significantly, and undoubtedly related to the disappearance of scurvy present in 1870 was that in 1872 or 1873 a garden of 40 acres provided fresh vegetables until about August each year. Fresh vegetables were still lacking during the winter. The nearest settlement for obtaining fresh vegetables was 75

Table 5
FORT SILL—1874

DISCHARGES	
"Disability"	
Chronic Bronchitis	
Valvular Heart Disease	
Valvular Heart Disease	
Valvular Heart Disease	
Puncture Wound Chest	
WOUNDED	
Gunshot wound (Accidental)	
DEATHS	
Valvular Disease Heart	
Purpura	
Congestive Intermittent Fever	
Chronic Dysentery	
Bright's Disease	
Suicide	
Exhaustion following attack	
Typho-Malarial Fever	
Inflammation of Endocardium	
Consumption	

miles distant. The post garden was in the northeast corner of the post just below the bluff. Highway 281 now runs through the site of the garden.

Of as great interest as the summaries given by Kilbourne and Brown are a list of discharges from service and deaths given by the post surgeons in the monthly reports.[7] Some of these have been tabulated in Table 5 and for the first time is noticed a condition which took a terrific toll in the next several years: Valvular disease of the heart (including inflammation of the endocardium). The large number of these cases must reflect the prevalence of streptococcal infections (not by any means necessarily during military service) and resultant rheumatic fever. One wishes for a more complete description of the cases listed as "rheumatism." This table also makes the first allusion to consumption which was to be so devastating a short time later among the Indians now settled upon the reservation.

Thus, the years 1870-1875 at Fort Sill were at best extremely hazardous. The greater danger from disease compared to battle casualties is starkly seen in the health figures. Fort Sill (along with Fort Gibson) gained a reputation as a particularly unhealthy post, especially in regard to malaria. During this period one obtains a picture of energetic and knowledgeable physicians and medical and military historians. Two in particular appear to be men of unusual qualities: Justus M. Brown (Assistant Surgeon 1870-1874) and Francis L. Town (Surgeon 1874-1878). A biographical study of these two pioneer "Oklahoma" physicians would prove of great interest. Their observations of the relationship of garbage disposal and water contamination to disease were correct. The hypothesis that the diseases were caused by "emanations" (miasms) of course could be proved incorrect only after the development of microbiology. The parallel between these incomplete concepts and our present day concepts of cancer and atherosclerosis is striking. □

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News From The Oklahoma State Department of Health

LOCUST GROVE HEPATITIS EPIDEMIC—WHY?

In early December of 1971 the State Health Department received reports of an unusual number of cases of infectious hepatitis from the Locust Grove, Oklahoma area. Over the next few days an epidemic was identified in which over fifty cases of the disease were documented. Approximately fifty additional cases of illness, clinically compatible with infectious hepatitis but not documented as such, also occurred during this period. The ratio of subclinical to clinical cases has been estimated at approximately three to one. The total number of cases may have been considerably greater than the number documented.

It is of considerable interest that in the months prior to this epidemic, water samples from the Locust Grove municipal water supply revealed unsatisfactory counts of bacteria, including fecal coliforms. In addition, several physicians in the area reported seeing unusual number of cases of a "diarrheal illness" in the community in the weeks and months prior to the hepatitis epidemic.

The city's water supply consists of four wells and a free flowing spring. Tests of the various components of the water system have shown the four wells to be satisfactory bacteriologically. Heavy contamination of the spring has been documented however.

A fair question to ask at this point is how a known health risk escaped official notice sufficiently long to result in a major epidemic of *preventable* disease. The State Health Department must step forward and take some blame in not *requiring* remedial action on the part of the city officials when water quality dropped below safe levels. City officials are guilty of laxity in response to water quality reports from the State Health Department laboratory. Finally, a number of area physicians are guilty of failure to comply with a state law requiring reports of specified communicable and infectious diseases. The Locust Grove epidemic escaped attention for many weeks because fewer than 25 percent of the cases seeing physicians were initially reported. □

COMMUNICABLE DISEASES IN OKLAHOMA FOR DECEMBER, 1971

Disease	Dec., 1971	Dec.. 1970	Nov.. 1971	Total to Date 1971	Total to Date 1970
Amebiasis	—	—	2	53	52
Brucellosis	—	1	1	5	9
Chickenpox	55	6	6	259	2524
Encephalitis, infect.	4	4	4	45	21
Gonorrhea	761	646	710	8318	6663
Hepatitis, infect. & serum	129	23	49	889	435
Leptospirosis	2	—	—	3	—
Malaria	—	10	—	68	113
Meningococcal infections	1	1	3	9	22
Meningitis, aseptic	1	1	2	118	44
Mumps	29	10	5	227	2405
Rabies in animals	11	9	3	281	97
Rheumatic fever	—	—	3	25	6
Rocky Mt. spotted fever	—	—	1	29	22
Rubella	—	4	1	70	826
Rubella, congenital syn.	—	—	—	—	—
Rubeola	1	156	1	795	947
Salmonellosis	11	14	13	193	165
Shigellosis	17	11	5	98	92
Syphilis	80	97	97	1230	1393
Tetanus	—	—	1	2	—
Tuberculosis, new active	21	35	21	324	344
Tularemia	3	—	—	20	8
Typhoid fever	—	—	—	3	1
Whooping cough	3	1	—	19	40

Continued from Page 43

cause they tend to throw statistics out the window and start with simple reasoning." Big words seemed to him only a camouflage of ignorance: "People think that if they have a name for a thing they understand it." Perhaps in no field of science is that more true than in medicine, where there is yet so much to learn.

But his greatest disdain was for the egotist. "Just the minute you get satisfied with what you've got, the concrete has begun to set in your head." To him the real trouble with the world was that "A few men want to be big shots and make everyone else serfs."

Since retirement from the active directorship of General Motors Research a dozen years ago, his time was devoted chiefly to three consuming interests. One was the famed Sloan-Kettering Institute which he and G. M. Chairman-of-the-Board Alfred P. Sloan established for cancer research, an interest which was no doubt spurred on by the death in 1946 of his beloved "Mrs. Ket," of cancer. A second became known as his "why the grass is green" investigation—(he was always asking why)—into the fundamental mechanism of the storage of solar energy by plants. This project was recently housed in a large modern laboratory building built by the Kettering Foundation on the campus of Antioch College at Yellow Springs, Ohio. The third interest he had pursued for more than fifty years, ever since his boyhood wonderment on the mystery of how a magnet can exert a pull on another object through space. The text-book explanation of "lines of force" which he was taught in his student years at Ohio State University did not quell his curiosity, which was insatiable and recognized no boundaries. Few people were aware that the trim white buildings located inconspicuously behind an Ohio farmhouse a few miles out of Dayton contained instruments for neutralizing the magnetic field of the earth and delving into properties of magnetism as yet unknown.

The tempo with which he pursued these projects was staggering. He commuted regularly between his home and New York City, Yellow Springs, and Detroit where he retained a position of leadership in General Motors affairs long after his retirement. Nearly all this travel was accomplished by air; he maintained three airplanes of his own and relaxed by taking over the controls from his pilots and flying himself, proud of the fact that he was one of the first licensed pilots in the United States and used to fly with his neighbors, the Wright Brothers. Occasionally there was time for a flight to "Far Horizons," the retreat which he built atop a knoll on the farm where he grew up near Loudonville, Ohio, or to Alabama or Florida for work on other research projects. He was still maintaining this schedule when, at the age of 82, he died unexpectedly at home in Dayton, a few days before Thanksgiving.

Mr. Kettering was an earnest worker, a Lincolnesque story teller with a dynamic, yet warm and friendly manner. His modesty was genuine. His wealth, acquired in the best American tradition, he regarded as a means of contributing to the progress of mankind. Characteristically he looked not to past accomplishments but to the future "because that's where we are going to be spending the rest of our lives." About that he was always optimistic: "With willing hands and open minds, the future will be greater than the most fantastic story you can write. You will always under-rate it."

These are the distillate of a great mind. Medicine owes a vast debt to leaders from other fields, such as "Boss Ket," who provide their unique wisdom, vision and stimulus to our profession.—*Dale Groom, MD*

Department of Medicine, University of Oklahoma Health Sciences Center, 800 N.E. 13th Street, Oklahoma City, 73104. □

1. Jour. S. C. Med. Assoc. 36, Jan. 1959.
2. J.A.M.A. 167: 1360, July 12, 1958.

Annual Meeting To Stress Social and Economic Change

Changes being wrought on the practice of medicine by social and economic pressures will be the main topics of discussion during the OSMA's 66th Annual Meeting. Scheduled for May 18th-20th, the meeting will be held in Oklahoma City's Skirvin Hotel and the three days will be divided into five key portions.

Annual Meeting Chairman, John Blaschke, MD, pointed out that the practice of medicine is undergoing some revolutionary changes that are not being brought about by scientific advancement, but by economic and sociological pressures. Since these changes are of vital concern to the medical profession, the annual meeting will be built around in-depth discussions of them. At the same time the program will not ignore the scientific aspects of continuing medical education.

The highlight of the scientific portion of the program will be Friday afternoon, May 19th, with a special Symposium on "Coronary Disease 72." A trio of speakers from the Mayo Clinic will conduct the seminar; Robert Brandenburg, MD; Daniel C. Connolly, MD; and Ralph Smith, MD.

In addition to this special seminar, all medical specialty societies are being invited to plan short seminars of specific interest to their own membership. These will be scattered throughout the three-day meeting.

The socioeconomic aspects of the program will be highlighted Saturday afternoon when four nationally prominent men will discuss "The Future of Medicine." Max Parrott, MD, from Oregon, is the knowledgeable and articulate Chairman of the AMA Board of Trustees and will lead the panel discussion. His presentation will be followed by the Former Deputy Executive Vice-President of the AMA, Richard Wilbur, MD, who is now an Under Secretary for Health Affairs in the United States Department of Defense.

One of the principle architects of Medicare, Wilbur J. Cohen, PhD, a nationally prominent social planner will follow Doctor Wilbur. The fourth member of the panel is a Former President of the United States Chamber of Commerce and the Editor and Publisher of the Tulsa Tribune, Jenkin Lloyd Jones. In addition to his other accomplishments, he is an internationally known syndicated columnist.

In announcing this particular portion of the program Doctor Blaschke said, "None of these men are timid. They are all nationally recognized for their knowledge, foresight, and especially for their forthrightness. We can expect nothing less than an extremely enlightening and lively discussion on Saturday afternoon."

The first of the socio-economic components of the annual meeting program will be held Thursday afternoon, May 18th, and will be a Third Party Payment Seminar. This is to be a "Nuts and Bolts" workshop for physicians or for the person in the physician's office responsible for billing third party carriers. Representatives from Aetna-Medicare, The Oklahoma Department of Institutions, Social and Rehabilitative Services (formerly DPW) and Oklahoma Blue Shield will be on hand to explain the operations of their various programs and to answer questions on such topics as proper filing of claims, changing of physician's fee profiles, contesting of payment decisions, justification of higher than usual fees, etc.

The importance of Peer Review is being discussed throughout the profession and will probably receive impetus from federal legislation since it is mentioned in almost every national health insurance proposal. A special "Symposium on Peer Review" will be held Friday morning, May 19th. A discussion on the philosophy of peer review from both the pro and con aspects will be presented. Three experts who are already working in peer review programs from other parts of the United States will be present.

Saturday morning, May 20th, will feature a symposium on "Health Maintenance Organizations." Popularly known as the HMO, this new concept in the delivery of health care services is being promoted by the Nixon Administration, the hierarchy of HEW, and a number of nationally known political figures. This discussion will revolve around what is an HMO, how does it work, how is it financed, and is it really "the answer" to health care delivery.

A major change in the business activities during the annual meeting has been planned. This year, the OSMA House of Delegates will hold its opening session on Thursday morning, May 18th. The reference committees for the House will meet Thursday afternoon, and the House will hold its closing session Thursday evening.

This change means that the meeting space available for Friday and Saturday can be devoted entirely to socioeconomic and scientific functions.

Two general social functions are planned for the 1972 meeting. A cocktail party will be held Friday evening, May 19th. Many specialty societies are planning to hold dinner meetings following the cocktail party.

During the President's Annual Dinner-Dance Saturday evening, May 20th, Lucien M. Pascucci, MD, Tulsa, will step down as President of the association and be replaced by Stanley R. McCampbell, MD of Oklahoma City, currently serving as President-Elect.

Provisions have been made for an exhibit area to house over 75 scientific and institutional exhibits . . . along with a few "recreational" exhibits. □

HIBAC Endorses Medicare Changes

HIBAC, the Health Insurance Advisory Council to Congress, has endorsed changes in the Medicare program in their annual report covering fiscal year 1971.

The council is composed of representatives of associations and organizations in the field of medicine, experts in the delivery and financing of health care, and representatives of consumers and the general public. Harlan Thomas, MD, of Tulsa, is a member of this important council.

HIBAC's responsibility is to advise the Secretary of Health, Education and Welfare on matters of general policy and on the formulation of regulations for the Medicare program. It also reviews the quality and utilization of health care under Medicare, and recommends legislative improvements in the program.

The council endorsed the following provisions of HR 1 . . . known as the Social Security Amendments of 1971, this bill has passed the House of Representatives and is now pending action in the United States Senate:

1. Authority for the Secretary of HEW to terminate or suspend Medicare payments to suppliers of health services found guilty of program abuse.
2. The option for Medicare beneficiaries to choose to have all covered care provided by a health maintenance organization.
3. Advance approval under Medicare of extended care and home health care.
4. Coordination of Medicare reimbursement with the findings of health facility planning bodies.
5. An in-depth review of methods of reimbursement for physicians' services under Medicare.
6. Establishment of a provider reimbursement review board to resolve disputes over reasonable cost determinations under Medicare.
7. A study to determine the desirability of covering chiropractic services under Medicare.

While endorsing most of the proposed Medicare changes embodied in HR 1, the council expressed unanimous opposition to the proposal to extend Medicare coverage to services of independently practicing physical therapists. It also recommended a broadening of the bill's provision to resolve Medicare provider-intermediary disputes, and for incentive reimbursement experimentation.

HIBAC has recommended that an explanation of the reasonable charge concept be included in the written notice to the beneficiary whenever medical insurance benefits have been paid on his behalf to the physician. In addition, whenever the amount of the physician's charge exceeds the amount determined to be reasonable under the law, the beneficiary is to be so notified. This is an apparent attempt on the part of the council to alleviate the hard feelings on the part of many over 65 patients when they receive their Medicare statement that simply says the physician's charge is "more than the allowable." The patient who does not understand the reasonable charge concept assumes that the physician has overcharged him. □

Research Survey Conducted in Muskogee

A medical research and health survey project is being conducted in Muskogee County by the Oklahoma Medical Research Foundation in cooperation with the Departments of Medicine, Biostatistics and Epidemiology of the University of Oklahoma Health Sciences Center. Researchers hope the study will reveal important new information about heart and lung diseases by identifying the frequency of hyperlipidemia and anti-trypsin.

Blood samples are being taken from a random six percent of the entire population of Muskogee County over 15 years of age. Persons who participated in the test were identified as normal or abnormal in terms of the two factors under study . . . lipids and anti-trypsin. A detailed analysis and interpretation was given to each volunteer and his physician with no charge.

Those found to be abnormal were asked to take a second test. If the adnormality was confirmed, the individual was asked to come to a clinic where a more extensive battery of tests would be administered, tests which were more appropriate for the abnormality.

Each volunteer was asked to complete a short questionnaire and then a small sample of blood was taken from a vein in the arm. The visit only required ten to fifteen minutes and light refreshments were served on completion of the tests.

Slightly more than 200 students of Muskogee High School were asked to participate. They were selected at random from the Sophomore, Junior and Senior Classes, and visited a mobile clinic on the school parking lot.

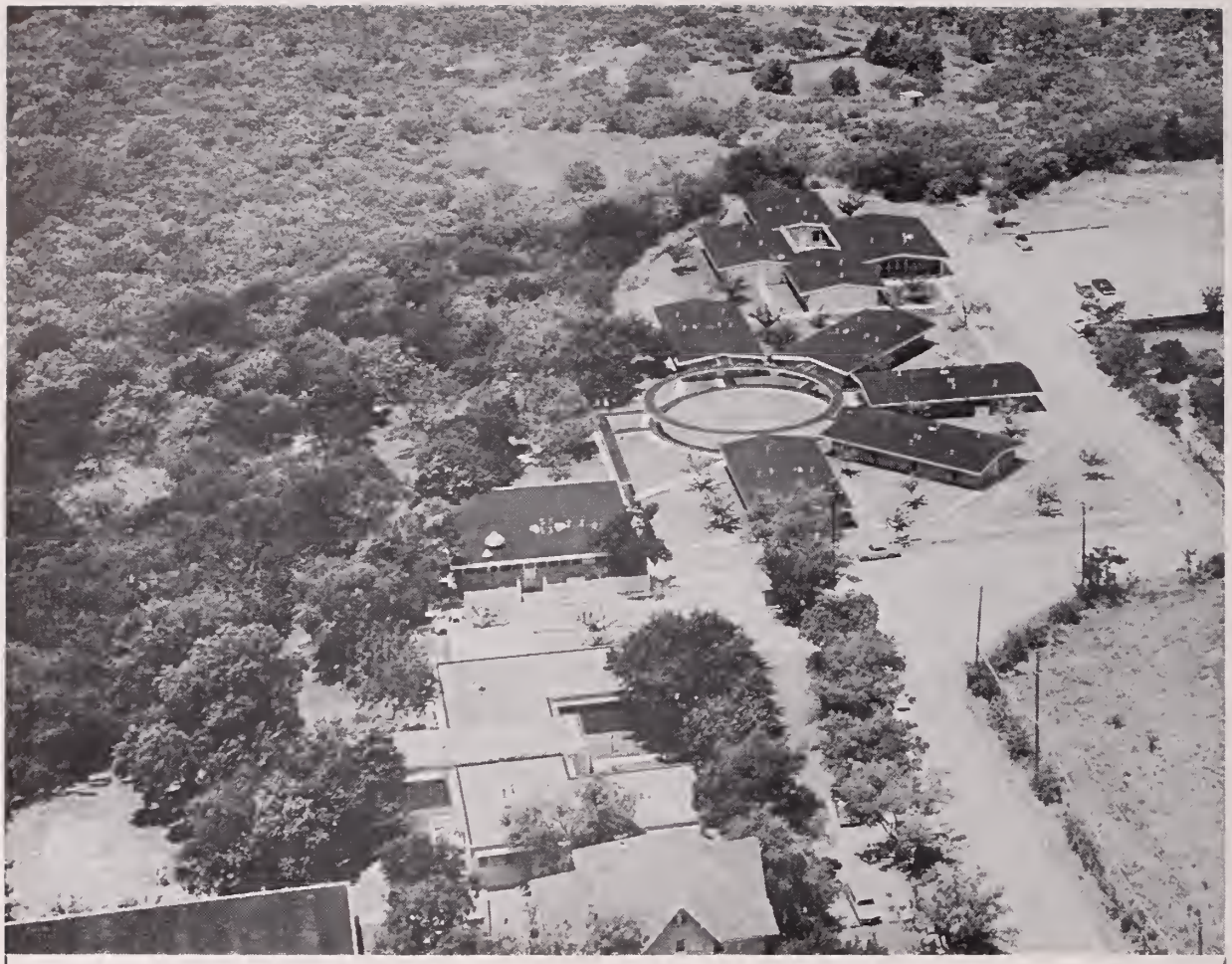
Muskogee County was one of two counties selected for the survey. A similar study was completed during December in Seminole County where officials described cooperation of the citizens as excellent.

The survey had the approval and endorsement of the Muskogee County Medical Society and was endorsed by the Oklahoma Heart Association and the Tuberculosis and Respiratory Disease Association with assistance from the Oklahoma State Health Department.

The lipid study was financed by the Oklahoma Medical Research Foundation, while the anti-trypsin study was supported by a grant to the University of Oklahoma Health Sciences Center from the National Heart and Lung Institute. □

Doctor Andrews Named Board President

Martin H. Andrews, MD, was elected President of the Board of Directors of the Deaconess Hospital, Oklahoma City, at the annual meeting of the group on January 17th, 1972. Doctor Andrews has been a member of the governing board of the hospital for several years, having served as Vice-President for the past three years. □



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Fee Schedules and Notice Posting

Physicians are required to prepare and maintain a fee schedule and post a notice that such a schedule is available for public inspection under recent regulations issued by the Price Commission. The schedule and posting requirement is a part of the Economic Stabilization Program.

The new regulation requires that each physician shall maintain at his office or offices a schedule showing "base prices for . . . principle services, and each change in such price." This price schedule is to be made available for public inspection, and a copy must be furnished to a representative of the Internal Revenue Service or the Price Commission if it is requested.

The regulation also requires that the physician shall post " . . . a sign in a prominent place in each (office) stating the availability and location of the schedule. No price may be increased before the sign is posted and the schedule is made available."

Unlike the regulations for retailers, those regarding physicians do not indicate a minimum size requirement for the price schedule sign that is to be posted. The IRS says only that the sign should be prominently displayed and easily readable. The wording could be as follows:

"In compliance with the Economic Stabilization Act a schedule of base price information for this office is available at the receptionist's desk."

The fee or price schedule itself can be handled in the following manner:

It is suggested that the physician list either the 40 service items which produce the highest gross income in his office, or the items which account for 50 percent of the practice gross income, if these are fewer than 40 items. Ordinarily, there are only three or four services in a physician's office which account for at least 50 percent of his income.

Two prices must be listed after each item on the schedule. The first price is the so-called "base price," this is the fee that was charged during the Wage-Price Freeze of August 16th through November 14th. The second price to be listed is the current fee being charged.

If a physician has raised his fee it must be indicated in the second column. However, the Price Commission has stated "the aggregate price increases of a (physician) may not exceed 2.5 percent a year." In addition, any price increase must be justified by increases in allowable costs incurred since the physician's last price increase or after January 1st, 1971, whichever is later. Any price increase must not "result in an increase in (the physician's) profit margin over that which prevailed during the base period." Also, before increasing his prices, a physician must take into consideration productivity gains.

Anyone having questions regarding the Price Commission's action should contact the Economic Stabilization Program at his local Internal Revenue Service office. The commission may be reached in Oklahoma City by telephoning Area Code 405, 231-4211. □

Assignment of Claims Explained by HEW

Confusion over what was the actual effect when a physician accepted an assignment of a Medicare claim caused the Health, Education and Welfare Department to issue new explanatory regulations.

In mid-1971 it was called to the attention of the state medical association that a number of physicians in Oklahoma were taking assignment and then billing the patient for whatever portion of the bill was not paid.

The new information states, "An assignment is an agreement between the physician and an enrollee. Under the terms of this assignment, the enrollee transfers to the physician his right to benefits based on covered services specified on the assigned claims: *the physician in return agrees to accept the reasonable charge determined by the carrier as his full charge for the items or services.*"

The italicized portion of the last quote is important. Whenever a physician accepts assignment he is precluded from charging the enrollee more than the deductible and co-insurance based upon the amount the carrier determines to be a reasonable charge . . . not the amount that he determines to be his fee. If he is dissatisfied with the determination of a reasonable charge as made by the carrier, he may request a review and a hearing, *"but he violates the assignment agreement if he collects (or attempts to collect) from the enrollee or anyone else any amounts, which, when added to the benefit, is in excess of the reasonable charge.* His bill for the service is paid in full when the reasonable charge is paid," the regulations state.

A number of physicians were inadvertently violating the regulations by collecting too much deductible. As an example, a physician would accept assignment on a bill for $300 and would collect $60 from the enrollee . . . the 20 percent co-insurance amount on $300. The carrier would then determine that a reasonable charge would be $250. At this point the physician had overcharged the enrollee since the 20 percent co-insurance on $250 would only be $50 . . . not the $60 that he had already collected. The difficulty arises since the physician must collect the co-insurance at the time the patient is in his office and may not know for several weeks what the carrier will determine to be a reasonable charge.

In the event that the physician does inadvertently overcharge the enrollee, the regulations require that he must reimburse the enrollee . . . or whoever paid the co-insurance . . . the overcharged amount.

In regard to private insurance the regulations state, "If the enrollee has private insurance in addition to Medicare, the physician who has accepted assignment of SMI benefits would be in violation of his assignment agreement if he bills or collects from the enrollee and/or the private insurer an amount which, when added to the Medicare benefit received, exceeded the reasonable charge."

Once a physician accepts an as-

signment, he cannot unilaterally rescind it. The regulations state that it "may be rescinded . . . before the carrier has made, and sent notice of, its reasonable charge determination."

Another portion of the new information says, "A physician may not accept assignment for some services, and claim payment from the enrollee for other services he performed for that same enrollee at the same place on the same occasion." This covers the situation where a physician would fragment his bill by accepting assignment on part of the services and billing directly on the remainder.

Officially the Oklahoma State Medical Association recommends that physicians not accept assignment and that they bill the patient directly. □

Two-Year Medical School Possible in Tulsa

A feasibility study conducted by the Booz, Allen & Hamilton Management Consultant Firm has recommened the creation of a two-year medical school in the Tulsa area. The report was commissioned by the Oklahoma Legislature and was the second to stress the importance of Tulsa to medical education.

The first report was issued in December by the Oklahoma Osteopathic Association and cited the feasibility of Tulsa as a location for a school of osteopathy. The latest report urges the establishment of a branch of the O. U. Medical School in Tulsa.

"In order to meet the physician needs in Oklahoma," the report stated, "a combination of actions will be required, including continued expansion of the University of Oklahoma College of Medicine, improvement and expansion of intern and residency programs and *the establishment of a two-year clinical medical school in Tulsa in affiliation with the University of Oklahoma.*"

Booz, Allen & Hamilton point out that Tulsa has adequate medical facilities to support the two-year clinical school and that the cost of developing and operating such a school is "substantially less than would be required for a classical four-year school."

Under the plan advanced the Oklahoma College of Medicine would admit 200 freshmen students each year. The students would take their first two years of basic science training on the Oklahoma City Campus of the Medical College. At the end of the sophomore year the class would be split into two groups of 100 each. One group would stay in Oklahoma City while the other went to Tulsa to complete their two years of clinical training.

One feature of the plan which is expected to make it very attractive to the Oklahoma Legislature is that there will be virtually no time-lag in the training of physicians since the entering class "at the University of Oklahoma College of Medicine could be expanded immediately for the basic science years. During the two years the students are receiving their basic science instruction, the clinical school at Tulsa could be organized and prepared to accept students beginning the third year."

It has often been estimated that it takes a minimum of ten years between the time a new medical school is conceived and the time its first student graduates. This time-lag would be cut in half if a two-year medical school plan is followed.

Operating costs for the Tulsa Clinical Medical School are estimated to amount to $1 million per year and will consist largely of faculty salaries and administrative and overhead expenses. Initially there will be no construction of major facilities since the basic science facility in Oklahoma City can accommodate an increased enrollment.

Faculty and administrative offices can be rented for several years and hospital facilities in the Tulsa area can be utilized for seminar and meeting rooms. Eventually, permanent facilities would be required for office space, laboratories, library facilities, and classrooms. It is estimated that adequate clinical and adminstrative facilties could be constructed for three to four million dollars.

"Initially, the Tulsa Medical School should have departments of internal medicine, general surgery, pediatrics, obstetrics/gynecology, psychiatry and community medicine/family practice," the report stated. "Each of the departments should have a fulltime director and geographic fulltime faculty. In addition, volunteer faculty will be required to supplement the geographic fulltime faculty. Radiology, pathology and anesthesiology experience would be acquired from the existing hospital departments."

The feasibility study calls for the Tulsa school to "develop innovative approaches to training physicians who will help meet the total needs of the state of Oklahoma, including physicians in family practice." It should strive to be innovative and experiment in developing medical education programs while not duplicating the efforts of the college of medicine in Oklahoma City.

To encourage the Tulsa school to develop independently of the college of medicine in Oklahoma City, the report calls for it to have its own dean "who should be responsible to the executive vice-president for health sciences as has been proposed by the administration of the Oklahoma Medical Center. This form of organization would give the Tulsa medical school the status it should have within the University of Oklahoma. . . ."

Expansion of the present medical school program should help to meet the demand for medical school admissions from Oklahoma residents as well as from non-residents of the state. In 1971, 332 Oklahomans applied for admission to the O. U. College of Medicine. Of that number, only 124 were admitted. In 1970, 123 Oklahomans who had applied for admission to medical schools somewhere in the United States were not admitted. While the qualifications of these students are not known the expansion of medical education programs in Oklahoma would enhance the possibility that they would gain admission to

a medical school if they are qualified.

While the report that was issued by the Osteopathic Association stressed that a four-year osteopathic school was feasible for Tulsa, the Booz, Allen & Hamilton report stated, "the development of a four-year medical school in Tulsa is not feasible at this time." The report then went on to stress the economic advantage to the state of expanding the O. U. program by adding the two year medical branch in Tulsa. □

Legislative Doctor Has Active "Practice"

Each day during the legislative session the OSMA furnishes a voluntary "Doctor of the Day" to treat the ills of Oklahoma's elected leaders and the employees of the State House and Senate. Since January 4th, over 25 physicians have handled the State House "practice."

Each Doctor of the Day serves one day in a special First Aid Station on the fourth floor of the State Capitol Building, located between the chambers of the two legislative bodies. The Senate and House of Representatives meet Monday through Thursday of each week during the Legislative Session.

The First Aid Station itself is equipped through voluntary contributions of drugs and supplies from various companies servicing doctors' offices. The drugs have been donated by the large pharmaceutical companies through their local detail men.

This year the majority of the non-drug supplies have been donated by Oklahoma Physician's Supply Company in Oklahoma City. Another Oklahoma City firm, Melton Company, Inc., has contributed to the station in the past.

Each day the doctor is on duty, there is also a "Nurse of the Day" to assist him. The registered nurse is a volunteer from the Oklahoma State Nurses Association.

Physicians from throughout the state are urged to volunteer to serve as "Doctor of the Day." Those interested should contact Mr. David Bickham, Associate Executive Director of the OSMA. □

Medical Students Seek Summer Employment

A summer employment program for medical students is being sponsored by the OSMA Medical Center Liaison Committee. The committee is asking each state association member to try to help at least one medical student find a medically related summer job.

Nearly 90 medical students have expressed a desire for summer employment and many have indicated they are willing to work in almost any Oklahoma community. The problem with summer jobs outside of Oklahoma City is usually one of housing.

The summer employment program allows a physician to gain a valuable part-time employee, and has the added advantage of enhancing the student's education by exposing him to the actual practice of clinical medicine.

Since most of the students are freshmen or sophomores, it is recommended that they be exposed to training in history taking and physical examination techniques and given experience in performing routine procedures based upon their individual competency, *e.g.*, blood pressure, vena punctures, scrub techniques, etc.

A monthly salary of $300/$350 during the June through August term of employment is recommended by the association. However, the final wage is negotiated directly between the physician-employer and the student on an individual basis.

All physicians wishing to employ students this summer should contact Ed Kelsay, Associate Executive Director of the OSMA. When the employment opportunity is received, it will be matched up with a student who has expressed a willingness to go to the community where the job is available, or to the student who meets the physician's requirements. The student will then be asked to contact the physician directly for a personal interview and negotiations on the job. □

Editor Receives Special Award

Mark R. Johnson, MD, Editor-in-Chief of *The Journal*, received a special award for his distinguished service as Chairman of the Regional Advisory Group, governing body of the Oklahoma Regional Medical Program.

The presentation was made January 14th, 1972, by Dale Groom, MD, Director of the ORMP, during the Advisory Group meeting in Oklahoma City.

Doctor Johnson has been a member of the Advisory Group since 1969 and Chairman since 1970. Members of the group recognized Doctor Johnson's leadership and wisdom which help to guide the program during its formative years and inspired the development of its present policy. □

Help For the Blind And Handicapped

The Oklahoma Library for the Blind and Physically Handicapped offers many services to aid physicians in the care of their handicapped patients. Located at 1108 N.E. 36th Street, Oklahoma City, the library is administered by the Department of Institutions, Social and Rehabilitative Services and serves the entire state.

Any individual who cannot read or turn the pages of a conventional book because of a disability may use the library services at his home or in the hospital.

To obtain the library privileges, a form, available from the library, must be signed by a competent authority such as a physician, a librarian, a professional staff member of a rehabilitation agency or the like.

At the library, magnetic tape, cassette and Braille books are also available. A print machine which will duplicate in large print, textbooks, music scores and other material for those who cannot cope with conventional size print is made available. □

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Cancer Forum To Convene in April

The Fourth Annual Arkansas-Oklahoma Cancer Forum will be held in Little Rock, Arkansas, at the University Medical Center on April 7th and 8th, 1972. This conveniently falls on Friday and Saturday, consisting of a day and a half of discussion about many timely controversial topics concerning the diagnosis and management of cancer patients. The subject material will be totally clinical and will be presented by experts from both the Arkansas and Oklahoma Medical Centers. Three of the speakers will be from regional and surrounding states. All discussants are recognized authorities in their field of interest, and should provide a highly stimulating learning experience.

Special arrangements have been made with the Sam Peck Hotel, whereby room rates will be reduced especially for this meeting. Wives can be registered at the hotel at no extra charge. The hotel is holding 150 rooms at these special rates.

Bus transportation will be furnished to and from the Sam Peck Hotel both Friday and Saturday. Buses will run to the Medical Center from the hotel, arriving in time for the morning sessions on Friday and Saturday, and returning to the hotel at the end of the scientific program, at approximately 4:30 p.m. on Friday, and at approximately 12:30 p.m. on Saturday. Buses will also be available to and from the hotel going to the Country Club of Little Rock for the "attitude changing hour" at 6:30 p.m. Friday. There will be no charge for the scientific meeting, but there will be a charge of $7.50 per person for the "attitude changing hour."

The Program

James L. Dennis, MD, Vice-President for Health Sciences at the Medical Center, University of Arkansas. will welcome all guests at 9:00 a.m. Friday morning.

The entire Friday morning will be devoted to gynecologic cancer. Doctor Gordon K. Jimerson, Oklahoma University Medical Center, will discuss border line and early invasive lesions of the cervix. Doctor James Merrill, Oklahoma University Medical Center, will discuss adenomatous hyperplasia of the endometrium and its relationship to cancer. Doctor Richard Boronow, University of Mississippi Medical Center, will discuss cancer of the endometrium and the final paper of the morning will be given by Doctor Roman-Lopez, University of Arkansas Medical Center. He will discuss early invasive cancer of the cervix and his preferred method of treatment. The final function will be a panel discussion concerning controversial subject material on gynecologic cancer, featuring the four morning speakers, and Doctor David Barclay, Professor of Gynecology, Arkansas Medical Center.

Doctor H. J. Sannan, area Vice-President for Medical Affairs of the American Cancer Society, will talk briefly about some human values in the treatment of cancer patients. The cancer society has recently placed increasing emphasis on the rehabilitation of the cancer patient.

The first discussion concerning melanoma will be by Doctor Thomas Jansen, Arkansas Medical Center. His discussion will concern the nature and diagnosis of this milagnancy. His talk will be followed by a film on the primary treatment of melanoma. This will be discussed by Doctor G. S. Campbell, Arkansas Medical Center.

Lymph node disection in melanoma and when it should be done is the third subject of discussion, which will be presented by Doctor Carl Knutson of the Ellis Fischel State Cancer Hospital of Columbia, Missouri. The final discussion about melanoma will concern palliative chemotherapy for advanced and recurrent disease. This discussion will be by Doctor William Tranum, Arkansas Medical Center. Following this, there will be a panel for questions and answers by the four afternoon mentioned essayists.

At 6:30 p.h. an "attitude changing hour" is scheduled at the Country Club of Little Rock. Hosts from Arkansas have planned an evening of relaxation, which should make the "change of attitude" quite painless.

On Saturday morning, the scientific session will convene again at the auditorium of the Medical Center. The subject material will be colon cancer with some pertinent recent observations about breast cancer.

Doctor Harvey Butcher, Professor of Surgery at Washington University School of Medicine in St. Louis, will discuss abdominal perineal resection vs. anterior resection for adenocarcinoma of the rectum and rectosigmoid. He will define when each operation should be properly carried out. The second discussion is about "no touch" technique for carcinoma of the colon. This will be presented by Doctor Knutson. He will describe in detail the procedure, and offer evidence of improved results with this technique.

A discussion of postoperative radiotherapy and adjuvant chemotherapy for cancer of the breast will be given by Doctor Harvey Butcher. The final formal presentation will be given by Doctor Knutson, and consists of a discussion of the proper treatment of Columbia class A and B adenocarcinoma of the breast. The final discussion of the symposium will be a panel consisting of Doctors Butcher, Knutson, Tranum, and Doctor John Broadwater about many of the controversial subjects which will have been raised by the individual presentations of the morning. □

Therapeutics Course Slated for March

A two-day postgraduate course on medical therapeutics will be held at the University of Oklahoma Health Sciences Center March 31st-April 1st, 1972. Several national authorities will participate in this general review of the use and abuse of several major drug categories as well as important recent advances in medical therapy. More detailed information is available through the Office of Continuing Medical Education for Physicians, University of Oklahoma Health Sciences Center, 800 N.E. 13th Street, Oklahoma City, Oklahoma 73190. □

Legislative Committee Pubishes Reporter

The OSMA Legislative Committee, chaired by R. Barton Carl, MD, has published its first Legislative Reporter for the 1972 session. The reporter lists bills of interest to the medical profession and gives the association's position on each one.

The following is a brief synopsis of the "most important bills" listed giving the bill number, author, a short explanation of what the bill does, and the OSMA's position.

SB 453 — Smith — Establishes a branch program of the School of Medicine in Tulsa County. Directs Higher Regents to allocate funds and authorizes the position of resident dean. The bill has been assigned to the Senate Committee on Higher Education and will probably be heard soon. (This bill was based on a report issued by the Booz, Allen & Hamilton Management Consultant Firm. An explanation of that report is contained on page 80 of this issue of *The Journal.)* OSMA Position: Support.

SB 112—Breckenridge—Repeals the Occupational and Professional Licensing Acts of 25 State Boards and Agencies including Medical Examiners. Creates new boards of five members, three of the profession—two laymen. Makes boards advisory while providing for a director appointed by the Governor. Senate Committee on Professions and Occupations. OSMA Position: Oppose.

SB 161—McSpadden—Provides for the removal and reappointment of members of the Board of Health. Creates a nine-man board consisting of four MDs, three DOs, one Dentist and one hospital administrator. This is almost identical to House Bill 1238. Assigned to the Senate Public Health Committee. OSMA Position: Oppose.

SB 458 — Breckenridge — Provides for abortions within 20 weeks after commencement of pregnancy if any of the following exist: That pregnancy would endanger the life or gravely impair the physical or mental health of the mother; that the child would be born with grave physical or mental defect; that the pregnancy resulted from rape or incest or illicit intercourse with a girl under 16 years of age—the abortion could be performed by a licensed physician in a medical clinic, approved hospital, or by the patient on advice of the physician. Assigned to Senate Committee on Public Health. OSMA Position: Oppose.

SB 461—Hamilton—Authorizes the State Regents for Higher Education to establish a school of osteopathy in Tulsa County. Appropriates $100,000 for planning and making the school operative. Reported "Do Pass" from Senate Committee on Higher Education and is on General Order in the Senate. OSMA Position: *The Committee hesitates to believe that State Government is willing and capable of financing three programs to train physicians, of the alternatives presented, the Branch Medical School is the most feasible. Therefore the committee opposes this legislation.*

HB 1423—Trent—Authorizes an insurance commissioner to prescribe standard reporting forms for accident and health insurance claims. Assigned to the House Insurance Committee. OSMA Position: Support.

HB 1500—Cate & Payne — Would require that all members of the healing arts licensed in Oklahoma pass a basic science exam equivalent to Oklahoma's exam. Assigned to the House Ways and Means Committee. OSMA Position: Support.

HB 1501—Cate & Payne—Would require that all members of the Healing Arts applying for a license in Oklahoma be graduates of a school approved by an accrediting agency recognized by the U. S. Office of Education. Assigned to the House Ways and Means Committee. OSMA Position: Support.

HB 1546—Elder—Reclassifies and adds certain drugs to Schedule II of the Uniform Controlled Dangerous Substances Act. Pentozocine is added to Schedule II and Amphetamine, Phenmetrazine and Methylphenidate are moved from Schedule II to Schedule III. In House on General Order. OSMA Position: Support

HB 1564—Willis—Appropriates $75,000 to the Oklahoma Rural Medical Education Loan & Scholarship Trust. OSMA Position: Support.

HB 1622—McCune—This legislation appears to place a complete ban on the importation and distribution of Amphetamines (Methamphetamine, Phenmetrazine, and Methylphenidite) in Oklahoma. It *does* provide for importation and distribution if approved by the Drug Treatment & Rehabilitation Authority. Assigned to House Judiciary Committee. The committee feels the bill is impractical to implement and impossible to enforce. OSMA Position: Oppose.

HB 1625—York—Makes substantial changes in the Chropractic Licensing Act; raises fees, adopts National Chiropcratic Examination and establishes a chiropractic scholarship fund. House Committee on Professions and Occupations. OSMA Position: Oppose. □

OMRF Lecturer Named

Sol Sherry, MD, Professor and Chairman, Department of Internal Medicine and Physician - In - Chief, Temple University School of Medicine and Hospital, Philadelphia, Pennsylvania, will present the third in a series of four Oklahoma Medical Research Foundation Lectures.

The lecture, entitled "Thrombosis," will be given at 4 p.m., March 14th, 1972 in the East and West Lecture Halls of the Basic Science Building, OU Health Sciences Center, Oklahoma City.

The Oklahoma Medical Research Foundation Lectures were established last year by the Board of Directors as a means of providing a valuable service to the practicing physicians of Oklahoma and to the staff of the OU Health Sciences Center.

The fourth and final lecture for fiscal 1971-72 will be the Second Annual Henry H. Turner Lecture in Endocrinology on April 11th, 1972. It will be given by George F. Cahill. MD, Professor of Medicine, Harvard University School of Medicine and Physician at Peter Bent Brigham Hospital, Boston, Massachusetts. □

Drug Abuse Treatment Film Now Available

Through a donation from the Hoffman-LaRoche Inc., the OSMA now has available for its members a 16mm color motion picture film on the emergency treatment of drug overdosed patients.

Entitled "What Did You Take?," the film was prepared by a New York production company to instruct physicians in the emergency treatment of overdoses of heroin, barbiturates, amphetamines, and LSD. It is designed for professional audiences only and is not recommended for the general public.

The film will be available to show to county medical societies, hospital staffs, and other qualified organizations by contacting the OSMA in Oklahoma City and requesting a showing date.

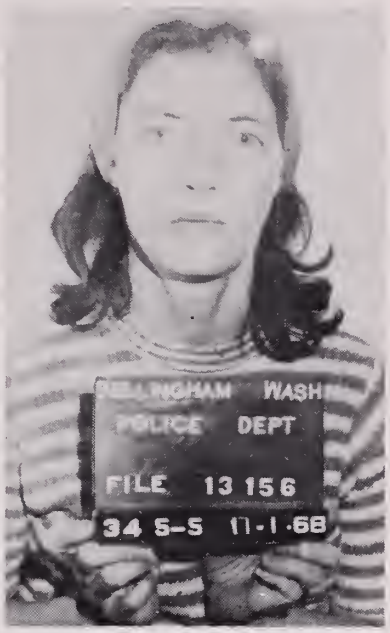
The donation from Hoffman-LaRoche was through its Roche Laboratories Division. This is the division that manufacturers two of the most widely used items in drug overdose treatment, the tranquilizers Librium and Valium. The donation was routed through Oklahoma's Department of Mental Health and its Director Hayden H. Donahue, MD.

One of the first uses of the new film will be by the Department of Mental Health to help train personnel working in the State Mental Health Hospitals.

In addition to the new movie, the association still has available a limited supply of its "Drug Abuse Treatment Manual." The manual was compiled and published under the direction of Charles Smith, MD, Chairman of the OSMA Alcoholism and Drug Abuse Committee.

Anyone wishing to obtain copies of the manual or seeking a showing date for the new film should contact Ed Kelsay, Associate Executive Director of the state medical association at 601 N. W. Expressway, Oklahoma City, Oklahoma 73118. □

Nurse's Aide Sought



The Federal Bureau of Investigation has asked *The Journal* to assist in alerting physicians and hospitals that Fern Ann Devoy is being sought by their department on charges of bond default resulting from her failure to appear in Federal Court on a charge of crime on a government reservation.

Mrs. Devoy is known to have worked as a nurse's aide on several occasions in the past. Her aliases include Fern Ann McCormick, Fern Ann Underhill and Mrs. Thomas Martin Devoy.

Any person having any information concerning Mrs. Devoy should contact the nearest office of the FBI immediately. No action should be taken which would endanger anyone's safety since Mrs. Devoy is considered as having suicidal tendencies. □

Clinical Anesthesiology For General Practitioners

The University of Oklahoma Health Sciences Center has announced a four-day course in clinical anesthesia for physicians who are not specialists in anesthesiology. Dates for the instruction are April 10th to 14th, 1972. Enrollment will be limited to those whose practice includes the administration of anesthetics.

The course will have to be limited by available clinical facilities. Total enrollment fee is $100.00. Applicants will be accepted for enrollment primarily on the basis of the sequence of arrival of the completed application forms which are available from the university. Each application must be accompanied by a deposit of $25.00. Remainder of the tuition is due by March 24th.

A one teacher to one student experience in the operating room will occupy the mornings during the course, while the afternoons will be involved with demonstrations and discussions.

Further information is available from the Department of Anesthesiology, University of Oklahoma Health Sciences Center, P.O. Box 26901, Oklahoma City 73190. □

Book Reviews

THE HUMAN HEART, A GUIDE TO HEART DISEASE. Brendan Phibbs, Associate Professor of Medicine, Department of Cardiology, University of Arizona School of Medicine, Tucson, Arizona. Second edition. 247 pp., with 72 illustrations. St. Louis: The C. V. Mosby Company, 1971. $5.75.

The author states this book is intended as a manual for patients who have heart disease themselves or for persons with medical training who are caring for someone with heart disease. The secondary purpose is to provide a paramedical textbook for nurses, aides and technologists involved in the care of cardiac patients.

The book fulfills the second purpose much better than its primary purpose. After a good beginning explaining the normal physiology of the heart in a straightforward manner, the book next attempts to explain what happens when the heart is diseased. Unfortunately, this is extremely difficult, if not impossible

to do in a simple way which can be readily understood by a person without medical training. As a test, I had an intelligent college graduate read the book and he had an extremely difficult time interpreting most areas beyond the basic chapters mentioned above.

Another major drawback of this book, in my opinion, is the lack of a glossary. There are many technical medical terms which are used repeatedly throughout the book and the only way to refresh one's memory of the meaning is to hunt through the index and contents to find where the word is defined.

This book may well be suited for use as a paramedical text as mentioned earlier. Its use for the nonmedical person is extremely limited by its complex nature and its attempt to cover too much in a too superficial manner. The parts of the book which are valuable for the patient appear to be the first nine chapters, the chapter on what to do about a heart attack and the small section on the general management of congenital heart disease. If a physician is going to use this book as a supplement to his practice, he is going to have to be highly selective in regard to the patients for whom it is used.—*Michael Grode, MD*

PROGESTERONE: ITS REGULATORY EFFECT ON THE MYOMETRIUM. Edited by G. E. W. Wolstenholme and Julie Knight, CIBA Foundation Study Group No. 34, J. and A. Churchill, London, 1969. 193 pp., illustrated. Available from the Williams and Wilkins Company, Baltimore.

This represents the proceedings of a CIBA Study Group held on May 14th, 1969, in memory of Brenda M. Schofield, MD, an outstanding worker in the area of progesterone blockage of myometrial activity. The membership of the study group included international authorities in the field of reproductive physiology, and the proceedings reflect their expertise and enthusiasm.

The study can be divided into three major areas, the regulation of myometrial function, uterine-ovarian interactions including hormonal biosynthesis, and the relation between uterine activity and feto-placental function.

Four interdependent, direct, controlling factors and the superimposed indirect actions of the maternal and fetal endocrine systems upon the myometrium are discussed in detail. The direct regulatory factors presented are (1) uterine volume, (2) oxytocin, (3) estrogen and (4) progesterone with the major emphasis being on progesterone suppression of uterine activity during gestation and the normal cycle.

This is an excellent review of the current concepts of progesterone influence on myometrial activity. The presentation of the material is suitable for both researcher and practitioner, and is a valuable reference for those interested in the possible hormonal mechanisms involved in the initiation of labor.—*O. Ray Kling, PhD*

CIBA FOUNDATION: MOLECULAR PROPERTIES OF DRUG RECEPTORS. Edited by Ruth Porter and Maeve O'Connor. Hardback. 298 pp., with 91 illustrations. London: J. & A. Churchill, 1970. Price (not stated).

Studies in molecular pharmacology are revealing in great detail that receptors are likely to be proteins, or at least that proteins are a very important part of receptors. To stress the importance of basing hypotheses about molecular mechanisms of drug-receptor interactions upon sound structural evidence, a three-day symposium was convened in London in 1970, with Doctor Francis H. C. Crick as its moderator. This volume represents the proceedings of the symposium, including a complete account of the formal presentations, the ensuing discussions and an excellent bibliography. The papers are divided into four groups. Of these, the first deals with the pharmacological properties of receptors, the second with the structure of active sites in enzymes, the third with conformational changes in proteins and what they can do, and finally, the fourth group which deals with the isolation and characterization of receptors themselves.

The contributors are authorities in their areas. The subject matter is advanced and is brought up to date by the participants. Clearly this is not a book which will help the practicing physician to more effectively prescribe drugs in the treatment of his patients. Rather this book summarizes certain highly advanced methods which are currently being applied to the solution of the complex problem of drug-receptor interactions on the molecular level. It will be appreciated most by basic scientists conversant with the most current, sophisticated developments in crystallography, nuclear magnetic resonance and fluorescent techniques, among others, who want to increase their comprehension on this subject.—*JoAnne I. Moore, PhD*

SO YOU HAVE GLAUCOMA. Everett R. Veirs, MD, New York, Grune & Stratton, 2nd edition, 1970. Clothbound, 84 pp., preface and table of contents. Eight illustrations and six pictures.

This modest little book was written with the express purpose of helping the patient with glaucoma to better understand his condition. After having received the shocking information that he/she has glaucoma, most patients seem unable to comprehend the explanation the ophthalmologist usually tries to give them and the importance of following therapeutic directions.

Following the preface the author presents a historical background of glaucoma after which he gives a good presentation of both the anatomy and the physiology of the eye as related to the increased intraocular pressure. In a logical sequence he then discusses the various types and causes of glaucoma, the subjective and objective signs of the disease, parameters used by the ophthalmologist to arrive at the

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Before

3/29/67 Before therapy with 5%-FU cream. Patient P. T. shows a moderately severe solar keratotic involvement. Note residual scarring from the previous cryosurgical and electrosurgical procedures on forehead and ridge of nose adjacent to periauricular area.

After

6/12/67 Seven weeks after cessation of therapy. Reactions have subsided. Residual scarring is not seen except for that due to prior surgery. Inflammation has disappeared and face is clear of keratotic lesions.



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Call it actinic, solar or senile keratoses, many regard it as "precancerous."[1,2]

Topical fluorouracil, considered by some dermatologists to be a major advance in the treatment of multiple solar keratoses,[3,4] offers the physician a relatively inexpensive alternative to cryosurgery, electrodesiccation and cold knife surgery. Of the topical fluorouracils available, only Efudex offers 2% and 5% solution and 5% cream formulations—formulations that have proved effective in the treatment of these mutliple lesions.

Usual duration of therapy, 2 to 4 weeks.

Studies showed that with the 2% and 5% Efudex preparations, the usual duration of therapy was only 2 to 4 weeks.[5] Other studies with topical fluorouracil revealed that when concentrations of less than 2% were used, significant numbers of lesions recurred.[6]

Treats the lesions you can't see, too.

Numerous lesions, not apparent prior to 2% and 5% Efudex therapy, manifested themselves by definite reactions, while intervening skin remained relatively unaffected.[5] The early eradication of these subclinical lesions (which may otherwise have undergone further progression) probably accounts for the reduced incidence of future solar keratoses in patients treated with topical fluorouracil—especially with 5% concentrations.[6]

How to identify solar keratoses.

Typically, the lesion—a flat or slightly elevated brown to red-brown papule—is dry, rough, adherent and sharply defined. Multiple lesions are the rule.

Predictable therapeutic response.

The response to a typical course of Efudex therapy is usually characteristic and predictable. After 3 or 4 days of treatment, erythema begins to appear in the area of keratoses. This is followed by a moderate to intense inflammatory response, scaling and occasionally moderate tenderness or pain. The height of this response generally occurs two weeks after the start of therapy and then begins to subside as treatment is stopped. Within two weeks of discontinuing medication, the inflammation is usually gone. Lesions that do not respond should be biopsied.

References: 1. Allen, A. C.: *The Skin, A Clinicopathological Treatise*, ed. 2, New York, Grune & Stratton, 1967, p. 842. 2. Dillaha, C. J.; Jansen, G. T, and Honeycutt, W. M.: "Treatment of Actinic Keratoses with Topical Fluorouracil," in Waisman, M. (ed.): *Pharmaceutical Therapeutics in Dermatology*, Springfield, Ill., Charles C Thomas, 1968, p. 92. 3. Belisario, J. C.: *Cutis, 6*:293, 1970. 4. Sams, W. M.: *Arch. Derm., 97*:14, 1968. 5. Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey. 6. Williams, A. C., and Klein, E.: *Cancer, 25*:450, 1970.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

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proper diagnosis, and also simplifies the various approaches employed in the treatment of the various types of glaucoma.

The author's style of writing for the lay patient is lucid and concise; but repetitious to the extent that what should be only a booklet has actually developed into a book, the size of which may deter the average patient from reading it. However, most ophthalmologists would accord gratitude to the author for the clarity of presentation in regards salient features of the disease condition, and the repeated explanations that there are several methods of diagnosis as well as forms of treatment — thereby discouraging glaucoma patients to "compare notes" which could result in their questioning the competence of either their own or the other patient's treating ophthalmologist.

This book may be recommended unreservedly to any patient who desires to become well informed about glaucoma.—*Wilmer A. Harms, MD*

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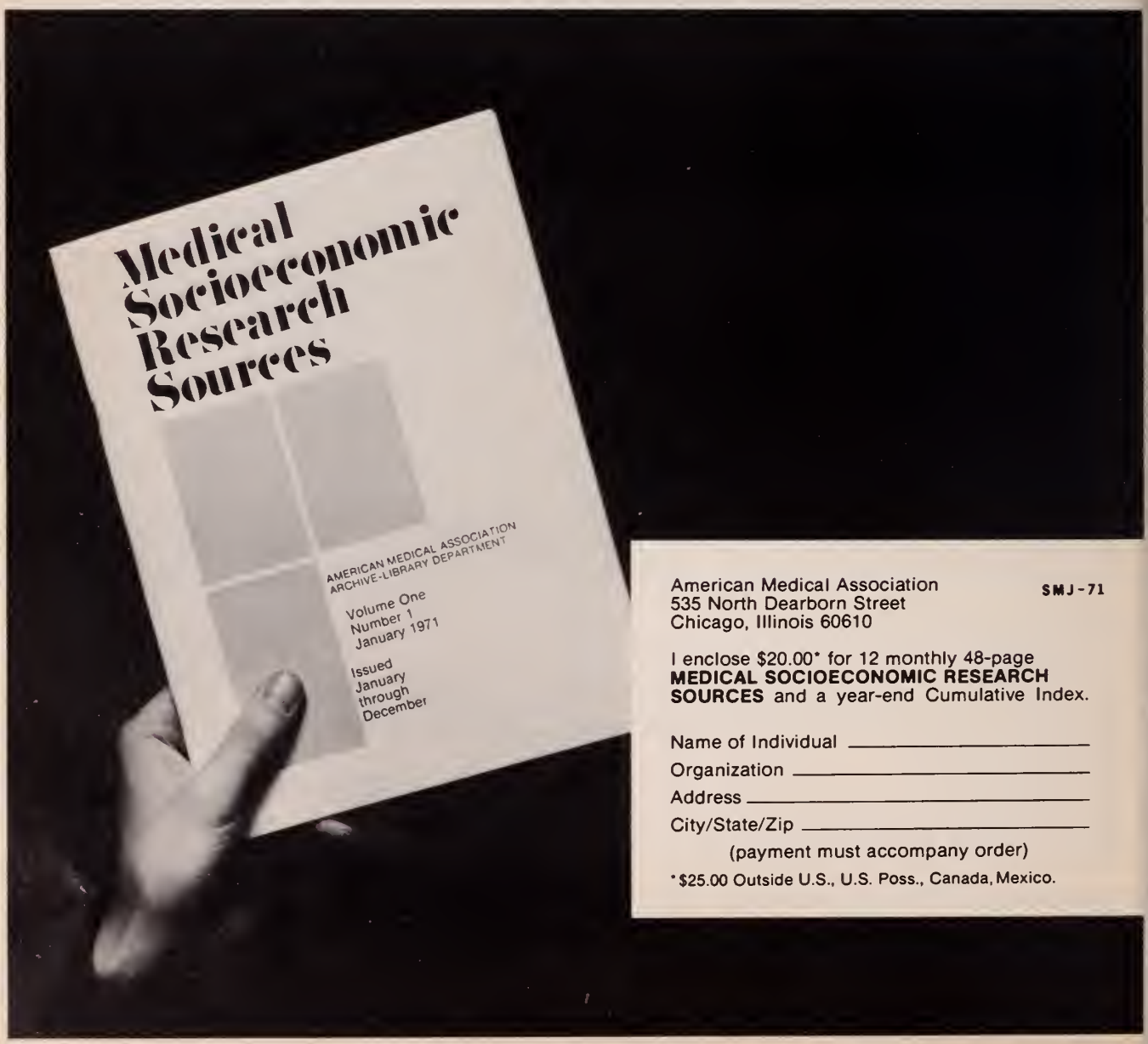
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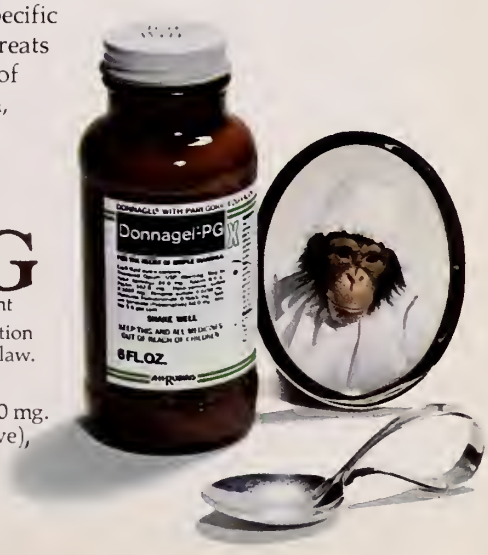
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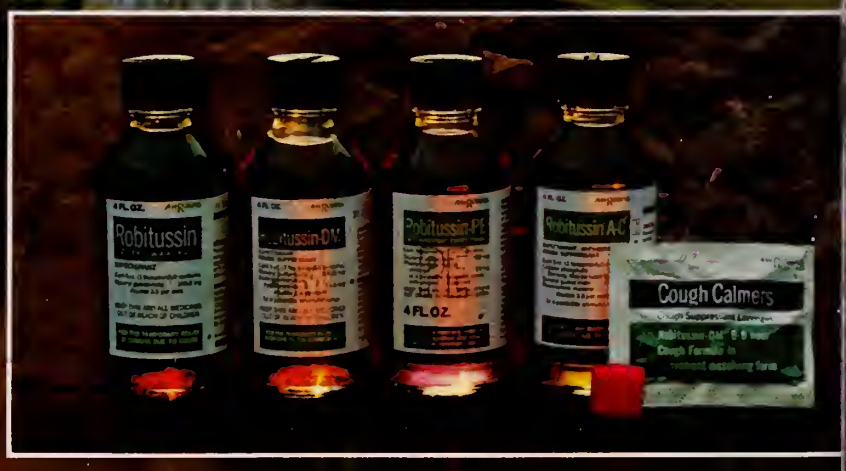
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T_4 IS THE PREDICTABLE HORMONE BECAUSE IT LOVES PROTEIN.

SYNTHROID® (sodium levothyroxine) is pure synthetic T_4, the major circulating thyroid hormone. It is reliable to use because of its affinity for protein-binding sites in the blood. T_3 is more fickle. Sometimes it binds. Sometimes it doesn't. T_4 more *predictably* binds to protein.

ALL THYROID-FUNCTION TESTS ARE USEFUL IN MONITORING SYNTHROID THERAPY

No calculations are needed, test interpretation is simple.

Any of the commonly used T_4 thyroid function tests (P.B.I., T_4 By Column, Murphy-Pattee, Free Thyroxine) are useful in monitoring patients on T_4 because they *all* measure T_4. Patients on SYNTHROID are thereby easy to monitor because their results will fall within predictable, elevated test ranges. Of course, clinical assessment is the best criterion of the thyroid status of the drug-treated patient.

TEST	HYPOTHYROID	SYNTHROID THERAPEUTIC NORMAL
P.B.I.	Less than 4 mcg %	6-10 mcg %
T_4 By Column	Less than 3 mcg %	7-9 mcg %
T_3 (Resin)	Less than 25%	27-35%
T_3 (Red Cell)	Less than 11%	11.5-18%
Free Thyroxine	Less than 0.7 nanograms %	0.7-2.5 nanograms %
Murphy-Pattee	Less than 2.9 mcg %	4-11 mcg %

TWO GOOD REASONS WHY THE ROAD TO NORMALIZED THYROID STATUS IS SO SMOOTH FOR THE SYNTHROID PATIENT.

(1) The onset of action of T_4 is gradual. It has a long in vivo "half-life" of over six days. (Occasional missed doses or accidental double-doses are of less concern because of this factor)[1]; (2) since SYNTHROID contains only T_4, the potential for metabolic surges traceable to more potent iodides (T_3) is eliminated.



AS WITH ANY THYROID PREPARATION, CAUTIOUS OBSERVATION OF THE PATIENT DURING THE BEGINNING OF THERAPY WILL ALERT THE PHYSICIAN TO ANY UNTOWARD EFFECTS.

Side effects, when they do occur, are related to excessive dosage. Caution should be exercised in administering the drug to patients with cardiovascular disease. Read the accompanying prescribing information for additional data or write Flint Laboratories.

Choose the Smooth Road ...to thyroid replacement therapy





ATIENTS CAN BE UCCESSFULLY IAINTAINED ON A RUG CONTAINING HYROXINE ALONE.

yroxine (T_4) is, as you know, e major circulating hormone oduced by the thyroid gland. is also produced, in smaller nounts, and is active at the llular level. For years it has been working hypothesis among ndocrinologists that T_4 is nverted by the body to T_3. In 70 this process, called iodination," was demonstrated Braverman, Ingbar, and Sterling[2]. does convert to T_3, though the ise quantities are still being ied.

The conversion has been nically demonstrated during the ministration of T_4 to athyrotic tients. Their thyroid status is rmalized on SYNTHROID alone, et the presence of T_3 in these atients has been clearly shown.

WHY DOES SYNTHROID COST LESS THAN SYNTHETIC DRUGS CONTAINING T_3?

Very simple. T_3 costs more to make synthetically than does T_4. So it is economically necessary for a synthetic thyroid medication containing T_3 to cost more than one containing T_4 alone. Synthetic combinations cost patients nearly 50% more than SYNTHROID[3] because the T_3 costs more to start with; also there is the additional expense of formulating a tablet containing two active ingredients.

1. Latiolais, C. J., and Berry, C. C.: Misuse of Prescription Medications by Outpatients, *Drug Intelligence & Clin. Pharm.* 3:270-7, 1969.
2. Braverman, L. E., Ingbar, S. H., and Sterling, K.: Conversion of Thyroxine (T4) to Triiodothyronine (T3) in Athyreotic Human Subjects, *J. Clin. Invest.* 49:855-64, 1970.
3. American Druggist BLUEBOOK, March, 1971.

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FACTS:
Synthetic thyroid drugs are an improvement over animal gland products. Patients, even athyrotic ones, can be completely maintained on SYNTHROID (T_4) alone. Thyroid function tests are easy to interpret since they are *predictably* elevated when the patient adheres to SYNTHROID. Of all synthetic thyroid drugs, SYNTHROID is the most economical to the patient.

A

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Indications: SYNTHROID (sodium levothyroxine) is specific replacement therapy for diminished or absent thyroid function resulting from primary or secondary atrophy of the gland, congenital defect, surgery, excessive radiation, or antithyroid drugs. Indications for SYNTHROID (sodium levothyroxine) **Tablets** include myxedema, hypothyroidism without myxedema, hypothyroidism in pregnancy, pediatric and geriatric hypothyroidism, hypopituitary hypothyroidism, simple (nontoxic) goiter, and reproductive disorders associated with hypothyroidism. SYNTHROID (sodium levothyroxine) **for Injection** is indicated for intravenous use in myxedematous coma and other thyroid dysfunctions where rapid replacement of the hormone is required. The injection is also indicated for intramuscular use in cases where the oral route is suspect or contraindicated due to existing conditions or to absorption defects, and when a rapid onset of effect is not desired.

Precautions: As with other thyroid preparations, an overdosage may cause diarrhea or cramps, nervousness, tremors, tachycardia, vomiting and continued weight loss. These effects may begin after four or five days or may not become apparent for one to three weeks. Patients receiving the drug should be observed closely for signs of thyrotoxicosis. If indications of overdosage appear, discontinue medication for 2-6 days, then resume at a lower dosage level. In patients with diabetes mellitus, careful observations should be made for changes in insulin or other antidiabetic drug dosage requirements. If hypothyroidism is accompanied by adrenal insufficiency, as Addison's Disease (chronic subcortical insufficiency), Simmonds's Disease (panhypopituitarism) or Cushing's syndrome (hyperadrenalism), these dysfunctions must be corrected prior to and during SYNTHROID (sodium levothyroxine) administration. The drug should be administered with caution to patients with cardiovascular disease; development of chest pains or other aggravations of cardiovascular disease requires a reduction in dosage.

Contraindications: Thyrotoxicosis, acute myocardial infarction. **Side effects:** The effects of SYNTHROID (sodium levothyroxine) therapy are slow in being manifested. Side effects, when they do occur, are secondary to increased rates of body metabolism; sweating, heart palpitations with or without pain, leg cramps, and weight loss. Diarrhea, vomiting, and nervousness have also been observed. Myxedematous patients with heart disease have died from abrupt increases in dosage of thyroid drugs. Careful observation of the patient during the beginning of any thyroid therapy will alert the physician to any untoward effects.

In most cases with side effects, a reduction of dosage followed by a more gradual adjustment upward will result in a more accurate indication of the patient's dosage requirements without the appearance of side effects.

Dosage and Administration: The activity of a 0.1 mg. SYNTHROID (sodium levothyroxine) TABLET is equivalent to approximately one grain thyroid, U.S.P. Administer SYNTHROID tablets as a single daily dose, preferably after breakfast. In hypothyroidism without myxedema, the usual initial adult dose is 0.1 mg. daily, and may be increased by 0.1 mg. every 30 days until proper metabolic balance is attained. Clinical evaluation should be made monthly and PBI measurements about every 90 days. Final maintenance dosage will usually range from 0.2-0.4 mg. daily. In adult myxedema, starting dose should be 0.025 mg. daily. The dose may be increased to 0.05 mg. after two weeks and to 0.1 mg. at the end of a second two weeks. The daily dose may be further increased at two-month intervals by 0.1 mg. until the optimum maintenance dose is reached (0.1-1.0 mg. daily).

Supplied: Tablets: 0.025 mg., 0.05 mg., 0.1 mg., 0.15 mg., 0.2 mg., 0.3 mg., 0.5 mg., scored and color-coded, in bottles of 100, 500, and 1000. Injection: 500 mcg. lyophilized active ingredient and 10 mg. of Mannitol, N.F., in 10 ml. single-dose vial, with 5 ml. vial of Sodium Chloride Injection, U.S.P., as a diluent. SYNTHROID (sodium levothyroxine) for **Injection** may be administered intravenously utilizing 200-400 mcg. of a solution containing 100 mcg. per ml. If significant improvement is not shown the following day, a repeat injection of 100-200 mcg. may be given.

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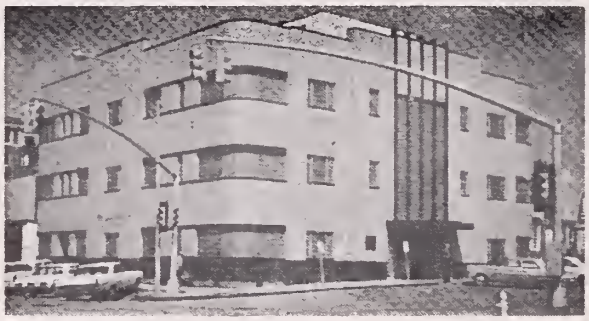
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The JOURNAL *of the Oklahoma State Medical Association*

DEADLINES

June Issue	
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Advertising Copy	May 15, 1972
News Copy, Miscellaneous Ads	June 1, 1972

CONTRIBUTIONS

Articles accepted for publication, including manuscripts of annual meeting papers, are the sole property of *The Journal* and must not have been published elsewhere. Authority for approval of all contributions rests with the Editorial Board, and the Board reserves the right to edit any material submitted. Manuscripts should be typewritten, double spaced and submitted in original and one copy. Receipt of manuscripts will be acknowledged and unused manuscripts returned. Used manuscripts will be returned on request. *The Journal of the Oklahoma State Medical Association* is not responsible for the statements or opinions of any contributor.

STYLE

Footnotes, bibliographies, and legends for illustrations should be submitted on separate sheets, double-spaced. Bibliographies should follow in order of: name of author, title or article, name of periodical with volume number, page and date of publication. These references should be alphabetized and numbered in sequence.

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NEWS

Members of the Oklahoma State Medical Association, the constituent societies of the association, and all readers in general are invited to supply news items of general interest to the profession.

ADVERTISING

All advertising copy must be approved by the Editorial Board before acceptance for publication. General and miscellaneous advertising rates will be sent on request.

EDITING SERVICE

The Editorial Board reserves the prerogative to submit contributions to a Medical Editing Service when warranted. If such is felt necessary, the Editor will contact the author for approval, informing him that there will be modest charge for this service.

REPRINTS

Authors will receive reprint order forms from the Transcript Press, P.O. Drawer 1058, Norman, Oklahoma 73069, prior to final publication of their articles. Other requests for reprints must be made to the Transcript Press within 30 days after publication.

BACK ISSUES

Microfilm copies of back issues of *The Journal* may now be purchased from University Microfilms, 300 North Zeeb Road, Ann Arbor, Michigan 48106.

HELP THE ECOLOGY:
DON'T THROW IT AWAY—
SAVE IT FOR IHA!

International Health Activities goal is to bring better health facilities to developing countries and under-privileged domestic areas, by seeing that nothing of medical use is discarded, but instead sent where it can be utilized; to involve our communities, our members, in providing these and other health necessities for the sick.

We continue our support for Project HOPE and want to tell you of two new activities:

1. *Wings for IHA.* The 99's, a women's flying group, will fly drugs (no narcotics), medical supplies, small equipment, PDRs, books and journals, bandages (sheets), scraps from old suits, johnny coats, soap, dolls from nylon stockings to Direct Relief Foundation in Santa Barbara, California. (This is off the record so if the information is incorrect or incomplete, let us know, but we have three of our members who are also members of 99's. They are Mrs. N. F. Wynn, Edmond; Mrs. Neil W. Woodward, Oklahoma City; and Mrs. R. M. Taliaferro, Ada.)

2. *Scholarships for Children of Indian Physicians.* A new and exciting approach for our Doctor's-Wife-to-Doctor's-Wife program comes to us from India. In many rural areas and small villages of this over-populated country there are no doctors or medical facilities of any kind. Yet in the large metropolitan areas there are many trained Indian physicians who would be willing to practice in these areas of need.

The salary of the native physician averages about $100 per month and this does not permit him to follow the Indian custom of sending his children to boarding schools for their education. Since there are no schools in the rural areas, he is forced to live and to practice medicine where his children can live at home while attending school.

The auxiliary, through Medical Assistance Programs, Inc., Box 50, Wheaton, Illinois 60187, is establishing a scholarship system for the children of such physicians. For $30 per month, which will completely finance a boarding school education for one child, you can "adopt" such a child, thereby releasing his physician father to practice in an area of greater medical need. This, in turn, may release an American volunteer physician to move on to another area of need.



Pictured (left) is Miss Subhashimala Mategaonker, 11, the child "adopted" by Dot Murray and Miss Shobha Mategaonker, 7, the child assigned to Eleanor Johnson. A brother of the sisters, Master Dinesh Mategaonker, 10, is pictured on the right.

Individuals wishing to "adopt" a child may send the money in monthly, quarterly or in annual installments. Or:

1. You may make installments as you are able and the money will be accumulated in your name until an entire year's schoarship is provided, at which time it will be awarded and contact established with the child and his family.

2. You may combine your funds with those of other individuals or auxiliaries to provide one or more scholarships.

We have been informed that of five adoptive parents as of this date, two of them are from Oklahoma. I would like to congratulate our State President, Dot Murray, and State President-Elect, Eleanor Johnson, for leading the way once again for all of us—not only in Oklahoma but also in our national organization.

Please contact Mrs. T. A. Ragan (Mary Jo), 730 Hoover St., Norman, Oklahoma 73069 for information on any of these programs. □

President Nixon's fiscal 1973 budget estimated federal spending on HEW Health Programs at $18.1 billion, an increase of $1.1 billion over the current fiscal year which ends next June 30th. The budget calls for a $49 million increase—to $435 million—for delivery of health services programs—health maintenance organizations, regional medical programs and health planning agencies. Medicare and Medicaid expenditures were increased by $492 million. The federal share of Medicaid was estimated at $3.4 billion or 55 percent of the total cost. Outlays for Medicare were estimated at $10.4 billion. The new cancer institute, functioning under the auspices of the National Institute of Health, came in for $430 million.

The cost of health care was the subject of the annual report to congress from the President's Council of Economic Advisors. The council cautioned that money alone does not hold the solution to the nation's health problems and stressed that new criteria for evaluating medical care should be developed. At the same time it pointed out that the nation's medical care expenditures totaled $75 billion —$358 per person—in fiscal year 1971, an annual growth rate of 4.3 percent per capita since 1966.

Oklahoma's Rex Kenyon, MD, has been elected to the AMPAC Board of Directors. He attended his first meeting of the board in mid-January where it was announced that the AMPAC membership reached a new record in 1971 for the fourth consecutive year, reflecting mounting physician interest in politics and governmental affairs.

The expected Bennett Amendment calling for the creation of "Professional Standards Review Organizations" was reintroduced in late January to be attached to HR 1, the Social Security Amendments of the 1971 bill. Senator Wallace Bennett (R-Utah) the sponsor, said the current amendment is "virtually identical" to that which he introduced in 1970. Medical societies, medical foundations or other organizations would be encouraged to submit plans for the establishment of PSROs. They would be responsible for review of medical services performed under Medicare and Medicaid "to assure that such services are medically necessary and meet proper quality standards." To qualify as a PSRO, an organization must be a voluntary and open its membership to all licensed MDs and Doctors of Osteopathy in a designated area. Membership in a medical society or other association may not be required. A national professional standards review council and a state PSRO would overlook the activities of the local PSRO.

Ralph Nader may have made his views on Chiropractic known recently. In mid-January he was scheduled to speak to a group of chiropractors attending a money making course offered by the Parker School for Professional Success in Dallas. According to the National Observer, when Nader found out that his speakers' bureau had scheduled him for the chiropractic event, he immediately cancelled the appearance.

HR 1, the Social Security Amendments for 1971, currently pending before the Senate Finance Committee is in for a batch of new amendments in addition to the one from Senator Bennett mentioned above. Senator Russell Long (D-La.) Chairman of the Committee is expected to use HR 1 as a vehicle for his national health insurance plan. It is expected that he will propose catastrophic health insurance for people under 65 years of age, that the federal government take over Medicaid, creation of a separate federal agency to administer Medicare and Medicaid, and provide for the expansion of Medicaid benefits and financing particularly in the area of mental health. He is expected to either second the Bennett Amendments or come up with his own professional standard review organization ideas. The senator has said he hopes to have the bill reported to the Senate floor by March 1st where it is expected to face lengthy debate. □

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Apr. 10-14	**Clinical Anesthesia for General Practitioners**
***Apr. 12**	**Endocrine Emergencies—Diabetic—Thyroid—Calcium**
Apr. 21-22	**Pathology, Radiology, Surgery Symposium—Diseases of the Thyroid**
Apr. 28-29	**Learning Disorders**
***May 11**	**Recent Advances in Cardiology**
May 12	**Association of House Staff Physicians—Annual Meeting**

For further information write:

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anxiety: a time bomb

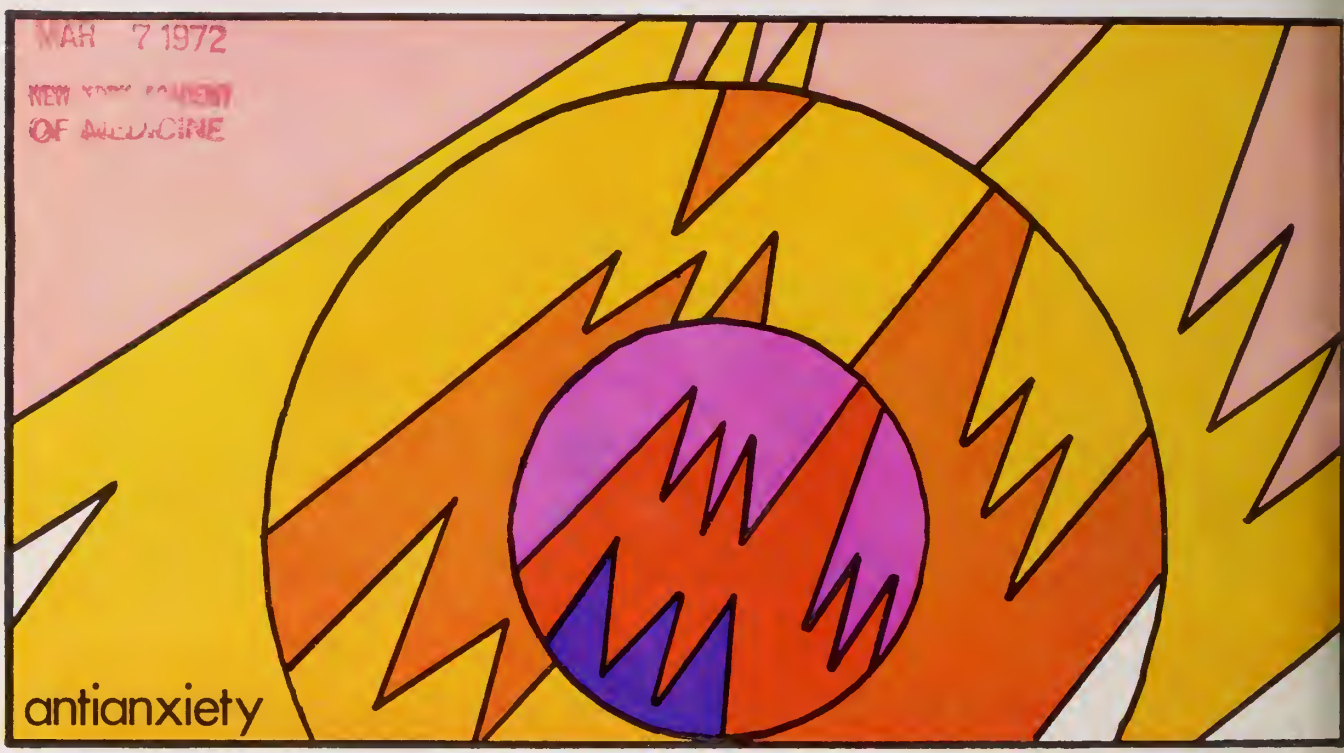
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Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances, syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

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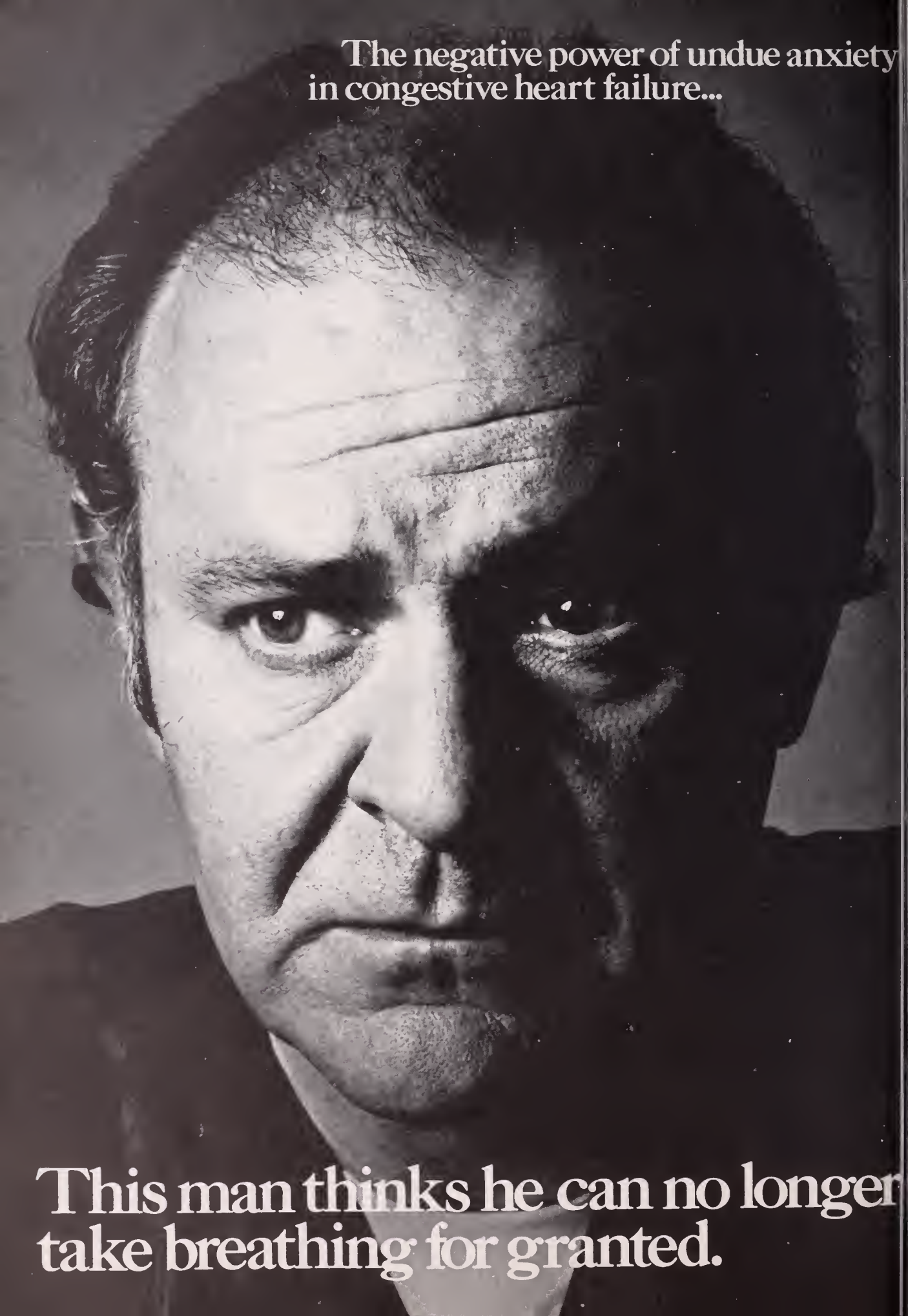
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JOURNAL
OKLAHOMA STATE MEDICAL ASSOCIATION

Volume 65—Number 3—March 1972



MARCH


The negative power of undue anxiety
in congestive heart failure...
This man thinks he can no longer
take breathing for granted.

Typical of many patients with congestive heart failure, he also suffers from severe anxiety, a psychic factor that may influence the character and degree of his symptoms, such as dyspnea. His apprehension may also deprive him of the emotional calm so important in maintenance therapy.

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Specific medical and environmental measures are often enhanced by the antianxiety action of adjunctive Libritabs (chlordiazepoxide). Libritabs can also facilitate treatment of the tense convalescent patient until antianxiety therapy is no longer required. Whereas in geriatrics the *usual daily dosage* is 5 mg two to four times daily, the *initial dosage* in elderly and debilitated patients should be limited to 10 mg or less per day, adjusting as needed and tolerated.

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All Mudranes are bronchodilator-mucolytic in action, and are indicated for symptomatic relief of bronchial asthma, emphysema, bronchiectasis and chronic bronchitis. **MUDRANE tablets** contain 195 mg. potassium iodide; 130 mg. aminophylline; 21 mg. phenobarbital (Warning: may be habit-forming); 16 mg. ephedrine HCl. **Dosage** is one tablet with full glass of water, 3 or 4 times a day. **Precautions** are those for aminophylline-phenobarbital-ephedrine combinations. **Iodide side-effects:** May cause nausea. Very long use may cause goiter. Discontinue if symptoms of iodism develop. **Iodide contraindications:** Tuberculosis; pregnancy (to protect the fetus against possible depression of thyroid activity). **MUDRANE-2 tablets** contain 195 mg. potassium iodide; 130 mg. aminophylline. **Dosage** is one tablet with full glass of water, 3 or 4 times a day. **Precautions** are those for aminophylline. **Iodide side-effects and contraindications are listed above. MUDRANE GG tablets** contain 100 mg. glyceryl guaiacolate; 130 mg. aminophylline; 21 mg. phenobarbital (Warning: may be habit-forming); 16 mg. ephedrine HCl. **Dosage** is one tablet with full glass of water, 3 or 4 times a day. **Precautions** are those for aminophylline-phenobarbital-ephedrine combinations. **MUDRANE GG-2 tablets** contain 100 mg. glyceryl guaiacolate; 130 mg. aminophylline. **Dosage** is one tablet with full glass of water, 3 or 4 times a day. **Precautions:** Those for aminophylline. **MUDRANE GG Elixir.** Each teaspoonful (5 cc) contains 26 mg. glyceryl guaiacolate; 20 mg. theophylline; 5.4 mg. phenobarbital (Warning: may be habit-forming); 4 mg. ephedrine HCl. **Dosage:** Children, 1 cc for each 10 lbs. of body weight; one teaspoonful (5 cc) for a 50 lb. child. Dose may be repeated 3 or 4 times a day. Adult, one tablespoonful, 4 times daily. All doses should be followed with ½ to full glass of water. **Precautions:** See those listed above for Mudrane GG tablets.

MUDRANE—original formula

First choice

MUDRANE-2

When ephedrine is too exciting or is contraindicated

MUDRANE GG

During pregnancy or when K.I. is contraindicated or not tolerated

MUDRANE GG-2

A counterpart for Mudrane-2

MUDRANE GG ELIXIR

For pediatric use or where liquids are preferred

Clinical specimens available to physicians.

WILLIAM P. POYTHRESS & COMPANY, INC., RICHMOND, VIRGINIA 23217

Manufacturers of Ethical Pharmaceuticals

The JOURNAL of the Oklahoma State Medical Association

MARCH
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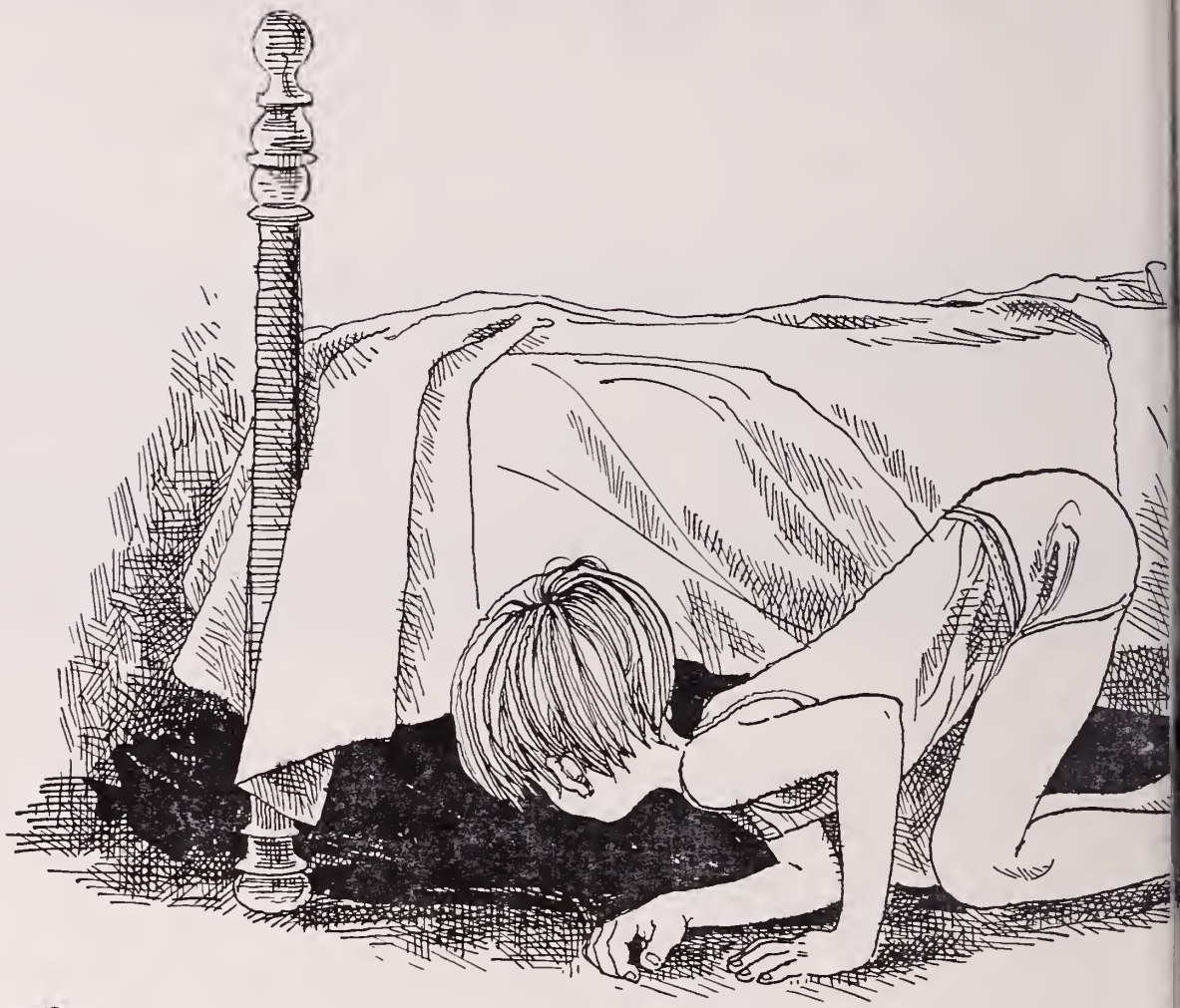
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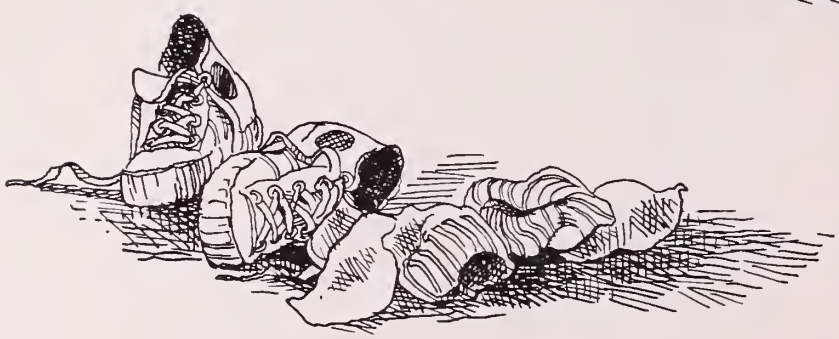
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Arthur lost





A single-dose, non-staining anthelmin

his pinworms...



with just one non-staining dose of Antiminth (pyrantel pamoate) Oral Suspension.

Highly effective. Active against pinworm...and roundworm.

Non-staining. Doesn't stain teeth or oral mucosa on ingestion. Doesn't stain stools, clothing or linen.

Simple dosage. Single-dose regimen: 1 cc. per 10 lbs. of body weight (1 tsp. per 50 lbs.).

Well-tolerated. Based on pre-introductory studies.

Pleasant-tasting. Easy-to-take, caramel-flavored oral suspension.

Economical. One prescription for the entire family.

Antiminth (pyrantel pamoate) Oral Suspension

Actions. Antiminth (pyrantel pamoate) has demonstrated anthelmintic activity against *Enterobius vermicularis* (pinworm) and *Ascaris lumbricoides* (roundworm). The anthelmintic action is probably due to the neuromuscular blocking property of the drug.

Antiminth is partially absorbed after an oral dose. Plasma levels of unchanged drug are low. Peak levels (0.05-0.13 μg/ml) are reached in 1-3 hours. Quantities greater than 50% of administered drug are excreted in feces as the unchanged form, whereas only 7% or less of the dose is found in urine as the unchanged form of the drug and its metabolites.

Indications. For the treatment of ascariasis (roundworm infection) and enterobiasis (pinworm infection).

Warnings. *Usage in Pregnancy:* Reproduction studies have been performed in animals and there was no evidence of propensity for harm to the fetus. The relevance to the human is not known.

There is no experience in pregnant women who have received this drug.

Precautions. Minor transient elevations of SGOT have occurred in a small percentage of patients. Therefore, this drug should be used with caution in patients with pre-existing liver dysfunction.

Adverse Reactions. The most frequently encountered adverse reactions are related to the gastrointestinal system.

Gastrointestinal and hepatic reactions: anorexia, nausea, vomiting, gastralgia, abdominal cramps, diarrhea and tenesmus, transient elevation of SGOT.

CNS reactions: headache, dizziness, drowsiness, and insomnia.

Skin reactions: rashes.

Dosage and Administration. *Children and Adults:* Antiminth Oral Suspension (50 mg. of pyrantel base/ml.) should be administered in a single dose of 11 mg. of pyrantel base per kg. of body weight (or 5 mg./lb.); maximum total dose 1 gram. This corresponds to a simplified dosage regimen of 1 cc. of Antiminth per 10 lbs. of body weight. (One teaspoonful = 5 cc.)

Antiminth (pyrantel pamoate) Oral Suspension may be administered without regard to ingestion of food or time of day; and purging is not necessary prior to, during, or after therapy. It may be taken with milk or fruit juices. Because of limited data on repeated doses, no recommendations can be made.

How Supplied. Antiminth is available as a pleasant tasting caramel-flavored suspension which contains the equivalent of 50 mg pyrantel base per ml., supplied in 60 cc. bottles.

gent: **new ANTIMINTH®**

(pyrantel pamoate)

equivalent to 50 mg pyrantel/ml

ORAL SUSPENSION

ROERIG Pfizer

A division of Pfizer Pharmaceuticals
New York, New York 10017



"Your dinner was perfect—from soup to 'Dicarbosil'."

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ANTACID
Write for Clinical Samples
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UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER OFFICE OF CONTINUING MEDICAL EDUCATION SHORT COURSE

APRIL 12th, 1972

ENDOCRINE EMERGENICES

Diabetic — Thyroid — Calcium — Adrenal

This half-day course in EndocrineEmergencies is designed for the general physician who wishes to refresh his knowledge in the field of endocrinology.

The course will focus on the recognition and treatment of the common endocrine emergencies and will include the following:

1. Survey of the most helpful diagnostic tests in the diagnosis of endocrine disorders will be emphasized.

2. Early recognition of the specific endocrine disorder with the idea of anticipating the crises and administering the appropriate therapy should the crises ensue.

Pre-Sate®
(chlorphentermine HCl)

CAUTION: Federal law prohibits dispensing without prescription.

Indications: Pre-Sate (chlorphentermine hydrochloride) is indicated in exogenous obesity, as a short term (*i.e.*, several weeks) adjunct in a regimen of weight reduction based upon caloric restriction.

Contraindications: Glaucoma, hyperthyroidism, pheochromocytoma, hypersensitivity to sympathomimetic amines, and agitated states. Pre-Sate (chlorphentermine hydrochloride) is also contraindicated in patients with a history of drug abuse or symptomatic cardiovascular disease of the following types: advanced arteriosclerosis, severe coronary artery disease, moderate to severe hypertension, or cardiac conduction abnormalities with danger of arrhythmias. The drug is also contraindicated during or within 14 days following administration of monamine oxidase inhibitors, since hypertensive crises may result.

Warnings: When weight loss is unsatisfactory the recommended dosage should not be increased in an attempt to obtain increased anorexigenic effect; discontinue the drug. Tolerance to the anorectic effect may develop. Drowsiness or stimulation may occur and may impair ability to engage in potentially hazardous activities such as operating machinery, driving a motor vehicle, or performing tasks requiring precision work or critical judgment. Therefore, such patients should be cautioned accordingly. Caution must be exercised if Pre-Sate (chlorphentermine hydrochloride) is used concomitantly with other central nervous system stimulants. There have been reports of pulmonary hypertension in patients who received related drugs.

Drug Dependence: Drugs of this type have a potential for abuse. Patients have been known to increase the intake of drugs of this type to many times the dosages recommended. In long-term controlled studies with high dosages of Pre-Sate, abrupt cessation did not result in symptoms of withdrawal.

Usage In Pregnancy: The safety of Pre-Sate (chlorphentermine hydrochloride) in human pregnancy has not yet been clearly established. The use of anorectic agents by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and child. Use of the drug during lactation is not recommended. Mammalian reproductive and teratogenic studies with high multiples of the human dose have been negative.

Usage In Children: Not recommended for use in children under 12 years of age.

Precautions: In patients with diabetes mellitus there may be alteration of insulin requirements due to dietary restrictions and weight loss. Pre-Sate (chlorphentermine hydrochloride) should be used with caution when obesity complicates the management of patients with mild to moderate cardiovascular disease or diabetes mellitus, and only when dietary restriction alone has been unsuccessful in achieving desired weight reduction. In prescribing this drug for obese patients in whom it is undesirable to introduce CNS stimulation or pressor effect, the physician should be alert to the individual who may be overly sensitive to this drug. Psychologic disturbances have been reported in patients who concomitantly receive an anorexic agent and a restrictive dietary regimen.

Adverse Reactions: Central Nervous System: When CNS side effects occur, they are most often manifested as drowsiness or sedation or overstimulation and restlessness. Insomnia, dizziness, headache, euphoria, dysphoria, and tremor may also occur. Psychotic episodes, although rare, have been noted even at recommended doses. **Cardiovascular:** tachycardia, palpitation, elevation of blood pressure. **Gastrointestinal:** nausea and vomiting, diarrhea, unpleasant taste, constipation. **Endocrine:** changes in libido, impotence. **Autonomic:** dryness of mouth, sweating, mydriasis. **Allergic:** urticaria. **Genitourinary:** diuresis and, rarely, difficulty in initiating micturition. **Others:** Paresthesias, sural spasms.

Dosage and Administration: The recommended adult daily dose of Pre-Sate (chlorphentermine hydrochloride) is one tablet (equivalent to 65 mg chlorphentermine base) taken after the first meal of the day. Use in children under 12 not recommended.

Overdosage: Manifestations: Restlessness, confusion, assaultiveness, hallucinations, panic states, and hyperpyrexia may be manifestations of acute intoxication with anorectic agents. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension, or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.

Management: Management of acute intoxication with sympathomimetic amines is largely symptomatic and supportive and often includes sedation with a barbiturate. If hypertension is marked, the use of a nitrate or rapidly acting alpha-receptor blocking agent should be considered. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard.

How Supplied: Each Pre-Sate (chlorphentermine hydrochloride) tablet contains the equivalent of 65 mg chlorphentermine base; bottles of 100 and 1000 tablets.

Full information available on request.

WARNER-CHILCOTT
Division, Warner-Lambert Company
Morris Plains, New Jersey 07950

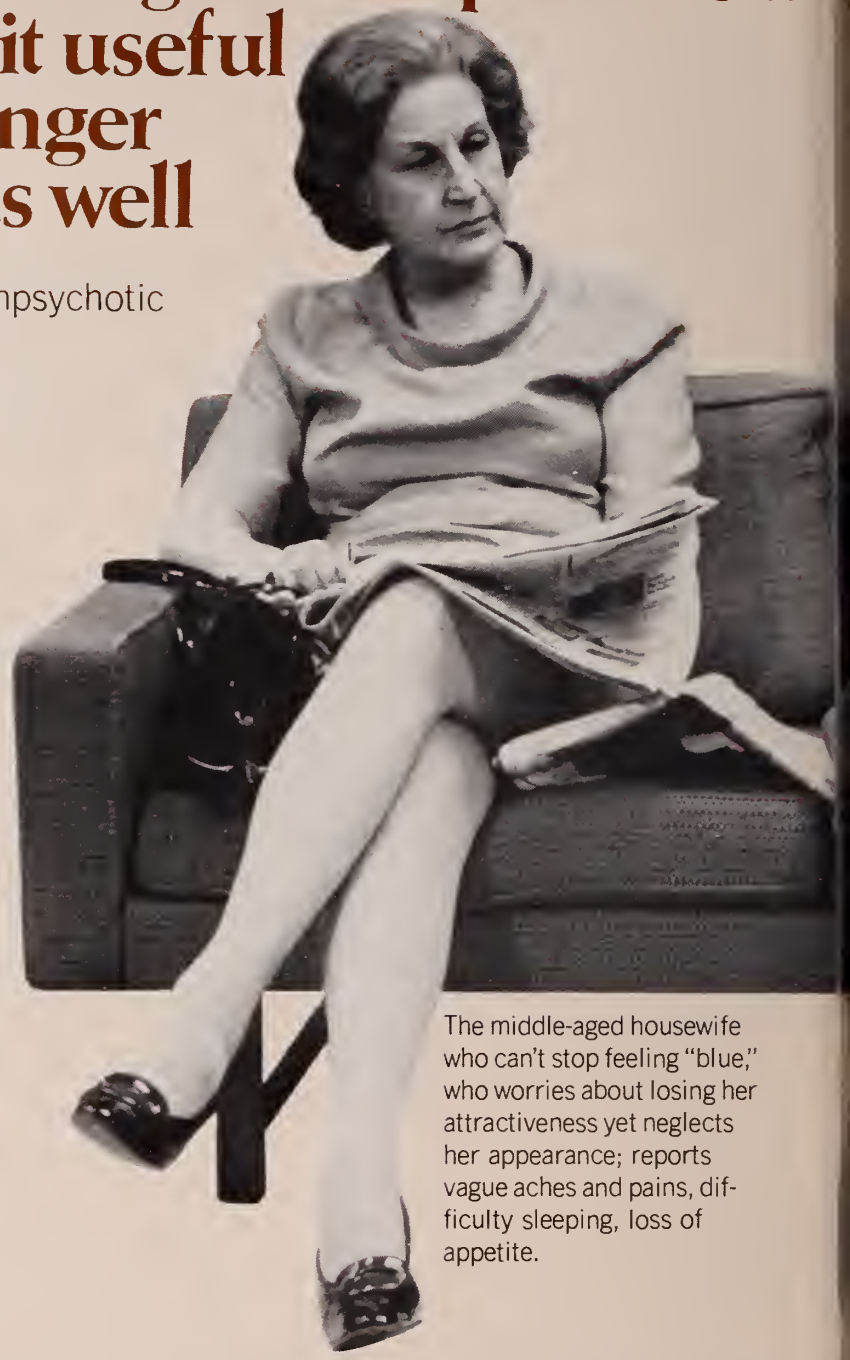


Pre-Sate® (chlorphentermine HCl)...the increasingly practical appetite suppressant



What makes 'Deprol' useful for depressed geriatric patients... makes it useful for younger patients as well

- helps ease mild to moderate nonpsychotic depression *and* related anxiety
- helps assure a good night's rest



The middle-aged housewife who can't stop feeling "blue," who worries about losing her attractiveness yet neglects her appearance; reports vague aches and pains, difficulty sleeping, loss of appetite.

INDICATIONS: Useful in the management of depression, both acute (reactive) and chronic; particularly useful in the less severe depressions and where the depression is accompanied by anxiety, insomnia, agitation, or rumination; also useful for management of depression and associated anxiety accompanying or related to organic illnesses.
CONTRAINDICATIONS: **Benactyzine hydrochloride:** Glaucoma and previous allergic or idiosyncratic reactions to benactyzine hydrochloride or related compounds. **Meprobamate:** Acute intermittent porphyria and allergic or idiosyncratic reactions to meprobamate or related compounds such as carisoprodol, mebutamate, tybamate, carbromal.
WARNINGS: The following information on meprobamate pertains to 'Deprol' (meprobamate + benactyzine hydrochloride): **Meprobamate:** *Drug Dependence:* Physical and psychological dependence and abuse have occurred. Chronic intoxication, from prolonged use and usually greater than recommended doses, leads to ataxia, slurred speech, vertigo. Carefully supervise dose and amounts prescribed, and avoid prolonged use, especially in alcoholics and addiction-prone persons. Sudden withdrawal after prolonged and excessive use may precipitate recurrence of pre-existing symptoms (e.g., anxiety, anorexia, insomnia) or withdrawal reactions (e.g., vomiting, ataxia, tremors, muscle twitching, confusional states, hallucinosis; rarely convulsive seizures, more likely in persons with CNS damage or pre-existent or latent convulsive disorders). Therefore, reduce dosage gradually (1-2 weeks) or substitute a short-acting barbiturate, then gradually withdraw. *Potentially Hazardous Tasks:* Driving a motor vehicle or operating machinery. *Additive Effects:* Possible additive effects between meprobamate, alcohol, and other CNS depressants or psychotropic drugs. *Pregnancy and Lactation:* Safe use not established; weigh potential benefits against potential hazards in pregnancy, nursing mothers, or women of childbearing potential. Animal data at five times the maximum recommended human dose show reduction in litter size due to resorption. Meprobamate appears in umbilical cord blood at or near maternal plasma levels, and in breast milk at levels 2-4 times that of maternal plasma. *Children Under Six:* Drug not recommended.
PRECAUTIONS: **Meprobamate:** To avoid oversedation, use lowest effective dose, particularly in elderly and/or debilitated patients. Consider possibility of suicide attempts; dispense least amount of drug feasible at any one time. To avoid excess accumulation, use caution in patients with compromised liver or kidney function. Meprobamate may precipitate seizures in epileptics.
ADVERSE REACTIONS: Nausea, dry mouth, other g.i. symptoms; syncope; one case each of severe nervousness and loss of power of concentration. The following side effects, which have occurred after administration of its components alone, have either occurred or might occur when the combination is taken. **Benactyzine hydrochloride:** Benactyzine hydrochloride alone, particularly in high dosage, may produce dizziness, thought-blocking, a sense of depersonalization, aggravation of anxiety, or distur-

When mild depression and associated anxiety interfere with living

DEPROL®

(meprobamate 400 mg + benactyzine hydrochloride 1 mg)



The junior executive crushed by his repeated failure to be promoted and anxious about the future; complains to you of listlessness, early-morning awakening.

The young widow whose grief has persisted too long, is pessimistic and fearful about what lies ahead, has lost interest in everything; is preoccupied with vague physical ailments, has crying spells.

bance of sleep patterns, and a subjective feeling of muscle relaxation. There may also be anticholinergic effects such as blurred vision, dryness of mouth, or failure of visual accommodation. Other reported side effects have included gastric distress, allergic response, ataxia, and euphoria. **Meprobamate:** *Central Nervous System:* Drowsiness, ataxia, dizziness, slurred speech, headache, vertigo, weakness, paresthesias, impairment of visual accommodation, euphoria, overstimulation, paradoxical excitement, fast EEG activity *Gastrointestinal:* Nausea, vomiting, diarrhea. *Cardiovascular:* Palpitations, tachycardia, various forms of arrhythmia, transient ECG changes, syncope; also, hypotensive crises (including one fatal case). *Allergic or Idiosyncratic:* Usually after 1-4 doses. Milder reactions: itchy, urticarial, or erythematous maculopapular rash (generalized or confined to groin). Others: leukopenia, acute nonthrombocytopenic purpura, petechiae, ecchymoses, eosinophilia, peripheral edema, adenopathy, fever, fixed drug eruption with cross reaction to carisoprodol, and cross sensitivity between meprobamate/mebutamate and meprobamate/carbromal. More severe, rare hypersensitivity: hyperpyrexia, chills, angioneurotic edema, bronchospasm, oliguria, anuria, anaphylaxis, erythema multiforme, exfoliative dermatitis, stomatitis, proctitis, Stevens-Johnson syndrome; bullous dermatitis (one fatal case after meprobamate plus prednisolone). Stop drug, treat symptomatically (e.g., possible use of epinephrine, antihistamines, and in severe cases corticosteroids). *Hematologic:* Agranulocytosis and aplastic anemia (rarely fatal), but no causal relationship established. Rarely, thrombocytopenic purpura. *Other:* Exacerbation of porphyric symptoms.

USUAL ADULT DOSAGE: One tablet three or four times daily, which may be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended.

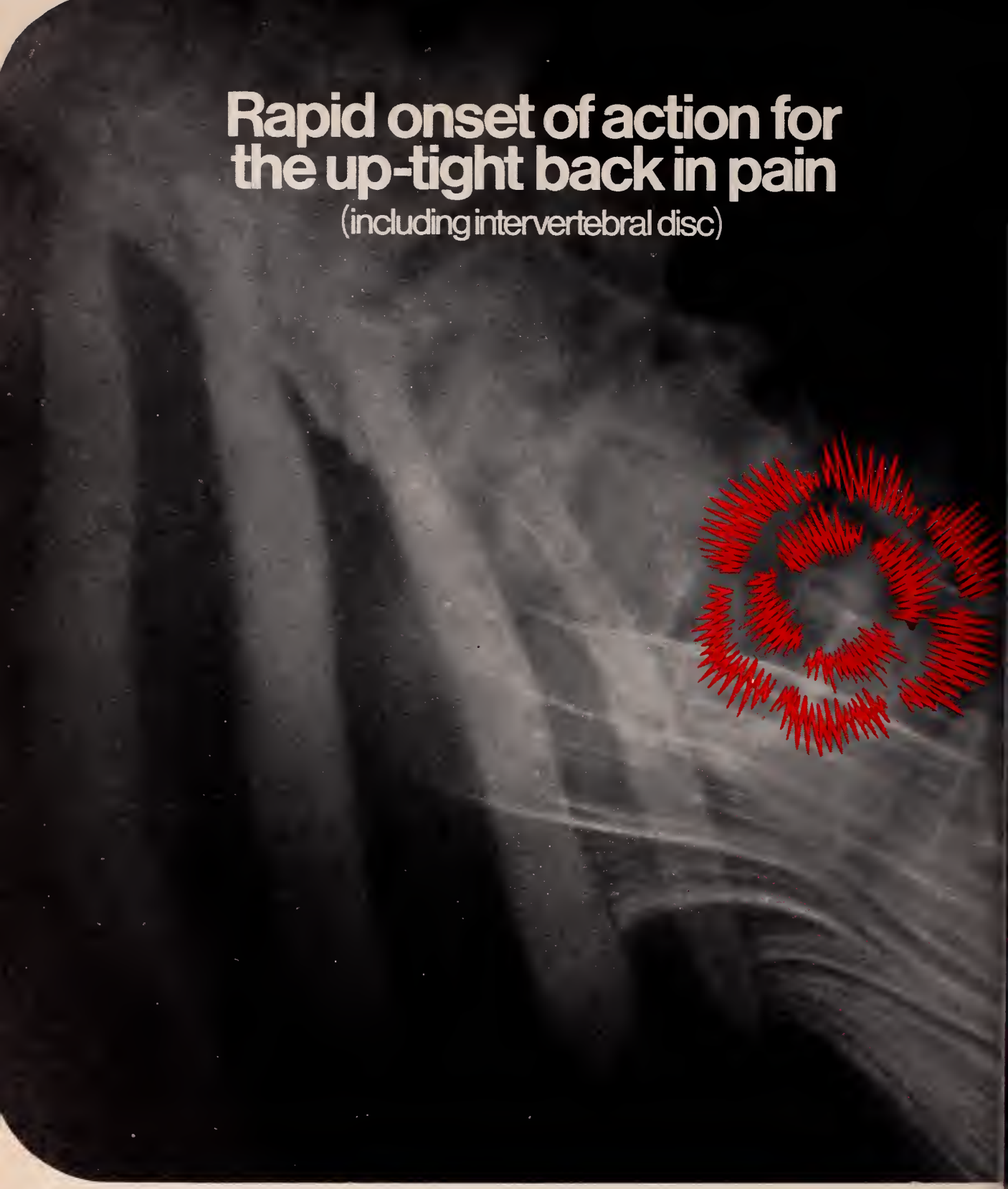
OVERDOSAGE: Overdosage of 'Deprol' (meprobamate + benactyzine hydrochloride) has not differed substantially from meprobamate overdosage: **Meprobamate:** Suicidal attempts with meprobamate, alone or with alcohol or other CNS depressants or psychotropic drugs, have produced drowsiness, lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse, and death. Empty stomach, treat symptomatically; cautiously give respiratory assistance, CNS stimulants, pressor agents as needed. Meprobamate is metabolized in the liver and excreted by the kidney. Diuresis and dialysis have been used successfully. Carefully monitor urinary output; avoid overhydration; observe for possible relapse due to incomplete gastric emptying and delayed absorption. REV. 10/71

Before prescribing, consult package circular or latest PDR information.

WALLACE PHARMACEUTICALS, Cranbury, N.J. 08512

Rapid onset of action for the up-tight back in pain

(including intervertebral disc)



Indications: For symptomatic relief in conditions characterized by skeletal muscle spasm and mild to moderate pain.
Contraindications: Acute intermittent porphyria and allergic or idiosyncratic reactions to carisoprodol or related compounds such as meprobamate, mebutamate, tybamate.
Warnings: *Idiosyncratic Reactions:* Rarely, first dose has been followed by extreme weakness, transient quadriplegia, dizziness, ataxia, temporary vision loss, diplopia, mydriasis, dysarthria, agitation, euphoria, confusion, disorientation. Symptoms usually subside during the next several hours. Supportive and symptomatic therapy, including hospitalization, may be necessary. *Pregnancy and Lactation:* Safe use not established; weigh potential benefits against potential hazards in pregnancy, nursing mothers, or women of childbearing potential. *Children Under Five:* Drug not recommended. *Potentially Hazardous Tasks:* Driving a motor vehicle or operating machinery. *Additive Effects:* Possible additive effects between carisoprodol, alcohol, and other CNS depressants or psychotropic drugs. *Drug Dependence:* Use cautiously in addiction-prone patients.
Precautions: To avoid excess accumulation, use caution in patients with compromised liver or kidney function.
Adverse Reactions: *Central Nervous System:* Drowsiness, dizziness, vertigo, ataxia, tremor, agitation, irritability, headache, depressive reactions, syncope, insomnia. *Allergic or Idiosyncratic:* Usually seen after 1-4 doses in patients not previously exposed, e.g., rash, erythema multiforme, pruritus, eosinophilia, fixed drug



eruption with cross reaction to meprobamate. More severe manifestations: asthma, fever, weakness, dizziness, angioneurotic edema, smarting eyes, hypotension, anaphylactoid shock. Stop drug, treat symptomatically (e.g., possible use of epinephrine, antihistamines, and in severe cases corticosteroids). *Cardiovascular:* Tachycardia, postural hypotension, facial flushing. *Gastrointestinal:* Nausea, vomiting, hiccup, epigastric distress. *Hematologic:* Leukopenia and pancytopenia (on carisoprodol plus other drugs).

Usual Adult Dosage: One 350 mg tablet three times daily and at bedtime.

Overdosage: Has produced stupor, coma, shock, respiratory depression, and, very rarely, death. Overdosage of carisoprodol plus alcohol or other CNS depressants or psychotropic drugs can be additive. Empty stomach, treat symptomatically; cautiously give respiratory assistance, CNS stimulants, pressor agents as needed. Carisoprodol is metabolized in the liver and excreted by the kidney. Diuresis and dialysis have been used successfully with related drug meprobamate. Carefully monitor urinary output; avoid overhydration; observe for possible relapse due to incomplete gastric emptying and delayed absorption. REV. 10/71

WALLACE PHARMACEUTICALS / Cranbury, N.J. 08512

if skin is infected, or open to infection...

choose the topicals that give your patient–

- broad antibacterial activity against susceptible skin invaders
- low allergenic risk—prompt clinical response

Special Petrolatum Base
Neosporin® Ointment
(polymyxin B-bacitracin-neomycin)

Each gram contains: Aerosporin® brand polymyxin B sulfate, 5000 units; zinc bacitracin, 400 units; neomycin sulfate 5 mg. (equivalent to 3.5 mg. neomycin base); special white petrolatum q. s.
In tubes of 1 oz. and ½ oz. for topical use only.

Vanishing Cream Base
Neosporin®-G Cream
(polymyxin B-neomycin-gramicidin)

Each gram contains: Aerosporin® brand polymyxin B sulfate, 10,000 units; neomycin sulfate, 5 mg. (equivalent to 3.5 mg. neomycin base); gramicidin, 0.25 mg., in a smooth, white, water-washable vanishing cream base with a pH of approximately 5.0. Inactive ingredients: liquid petrolatum, white petrolatum, propylene glycol, polyoxyethylene polyoxypropylene compound, emulsifying wax, purified water, and 0.25% methylparaben as preservative.
In tubes of 15 g.

NEOSPORIN for topical infections due to susceptible organisms, as in impetigo, surgical after-care, and pyogenic dermatoses.

Precaution: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Contraindications: Not for use in the external ear canal if the eardrum is perforated. These products are contraindicated in those individuals who have shown hypersensitivity to any of the components.

Complete literature available on request from Professional Services Dept. PML.

Wellcome / **Burroughs Wellcome Co.**
Research Triangle Park
North Carolina 27709



the compound analgesic that calms instead of caffeinates

In addition to pain, this patient has experienced anxiety, fear, embarrassment, anger, and frustration. It's very likely that these psychic factors actually accentuated his perception of pain. Surely the last thing he needs is an analgesic containing caffeine. A much more logical choice is Phenaphen with Codeine. It provides a quarter grain of phenobarbital to take the nervous "edge" off, so the rest of the formula can control the pain more effectively. It's no accident that the Phenaphen formulations contain a sedative rather than a stimulant. Don't you agree, Doctor, that psychic overlay is an important factor in most of the accident cases you see?

A. H. Robins Company, Richmond, Va. A·H·ROBINS

Phenaphen® with Codeine

Phenaphen with Codeine Nos. 2, 3, or 4 contains: Phenobarbital (¼ gr.), 16.2 mg. (warning: may be habit forming); Aspirin (2½ gr.), 162.0 mg.; Phenacetin (3 gr.), 194.0 mg.; Hyoscyamine sulfate, 0.031 mg.; Codeine phosphate, ¼ gr. (No. 2), ½ gr. (No. 3) or 1 gr. (No. 4) (warning: may be habit forming).

Indications: Provides relief in severer grades of pain, on low codeine dosage, with minimal possibility of side effects. Its use frequently makes unnecessary the use of addicting narcotics. *Contraindications:* Hypersensitivity to any of the components. *Precautions:* As with all phenacetin-containing products, excessive or prolonged use should be avoided. *Side effects:* Side effects are uncommon, although nausea, constipation and drowsiness may occur. *Dosage:* Phenaphen No. 2 and No. 3—1 or 2 capsules every 3 to 4 hours as needed; Phenaphen No. 4—1 capsule every 3 to 4 hours as needed. For further details see product literature.

(III) Phenaphen with Codeine is now classified in Schedule III, Controlled Substances Act of 1970. Available on prescription and may be refilled 5 times within 6 months, unless restricted by state law.



Snifter working again

For upper respiratory allergies and infections including the common cold, Dimetapp Extentabs® effectively relieve the stuffiness, drip and congestion all night and all day long on just one Extentab every 12 hours. For most patients drowsiness or overstimulation is unlikely.

prescribing information appears on next page

A·H·ROBINS

A. H. Robins Company
Richmond, Va. 23220

Dimetapp® Extentabs

Dimetane® (brompheniramine maleate), 12 mg , phenylephrine HCl, 15 mg , phenylpropanolamine HCl, 15 mg

Dimetapp Extentabs®

INDICATIONS: Dimetapp Extentabs are indicated for symptomatic relief of allergic manifestations of upper respiratory illnesses, such as the common cold, seasonal allergies, sinusitis, rhinitis, conjunctivitis and otitis. In these cases it quickly reduces inflammatory edema, nasal congestion and excessive upper respiratory secretions, thereby affording relief from nasal stuffiness and postnasal drip.
CONTRAINDICATIONS: Hypersensitivity to antihistamines of the same chemical class. Dimetapp Extentabs are contraindicated during pregnancy and in children under 12 years of age. Because of its drying and thickening effect on the lower respiratory secretions, Dimetapp is not recommended in the treatment of bronchial asthma. Also, Dimetapp Extentabs are contraindicated in concurrent MAO inhibitor therapy.
WARNINGS: *Use in children:* In infants and children particularly, antihistamines in overdosage may produce convulsions and death.
PRECAUTIONS: Administer with care to patients with cardiac or peripheral vascular diseases or hypertension. Until the patient's response has been determined, he should be cautioned against engaging in operations requiring alertness such as driving an automobile, operating machinery, etc. Patients receiving antihistamines should be warned against possible additive effects with CNS depressants such as alcohol, hypnotics, sedatives, tranquilizers, etc.
ADVERSE REACTIONS: Adverse reactions to Dimetapp Extentabs may include hypersensitivity reactions such as rash, urticaria, leukopenia, agranulocytosis and thrombocytopenia; drowsiness, lassitude, giddiness, dryness of the mucous membranes, tightness of the chest, thickening of bronchial secretions, urinary frequency and dysuria, palpitation, hypotension/hypertension, headache, faintness, dizziness, tinnitus, incoordination, visual disturbances, mydriasis, CNS-depressant and (less often) stimulant effect, anorexia, nausea, vomiting, diarrhea, constipation, and epigastric distress.
HOW SUPPLIED: Light blue Extentabs in bottles of 100 and 500.

Continuing Medical Education Courses For Physicians

KEEP THIS CALENDAR

UNIVERSITY OF OKLAHOMA

HEALTH SCIENCES CENTER

Oklahoma City, Oklahoma

1972

The continuing education program for physicians of the University of Oklahoma Health Sciences Center has been granted full approval by the American Medical Association's Council on Medical Education.

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Apr. 10-14	**Clinical Anesthesia for General Practitioners**
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Apr. 21-22	**Pathology, Radiology, Surgery Symposium — Diseases of the Thyroid**
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May 11	**Recent Advances in Cardiology**
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For further information write:

Office of Continuing Medical Education for Physicians
University of Oklahoma Health Sciences Center
P. O. Box 26901
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T_4 IS THE PREDICTABLE HORMONE BECAUSE IT LOVES PROTEIN.

SYNTHROID® (sodium levothyroxine) is pure synthetic T_4, the major circulating thyroid hormone. It is reliable to use because of its affinity for protein-binding sites in the blood. T_3 is more fickle. Sometimes it binds. Sometimes it doesn't. T_4 more *predictably* binds to protein.

Synthroid®
(sodium levothyroxine)

ALL THYROID-FUNCTION TESTS ARE USEFUL IN MONITORING SYNTHROID THERAPY.

No calculations are needed, test interpretation is simple.

Any of the commonly used T_4 thyroid function tests (P.B.I., T_4 By Column, Murphy-Pattee, Free Thyroxine) are useful in monitoring patients on T_4 because they *all* measure T_4. Patients on SYNTHROID are thereby easy to monitor because their results will fall within predictable, elevated test ranges. Of course, clinical assessment is the best criterion of the thyroid status of the drug-treated patient.

TWO GOOD REASONS WHY THE ROAD TO NORMALIZED THYROID STATUS IS SO SMOOTH FOR THE SYNTHROID PATIENT.

(1) The onset of action of T_4 is gradual. It has a long in vivo "half-life" of over six days. (Occasional missed doses or accidental double-doses are of les concern because of this factor)[1]; (2) since SYNTHROID contains onl T_4, the potential for metabolic surges traceable to more potent iodides (T_3) is eliminated.

1. Latiolais, C. J., and Berry, C. C.: Misuse of Prescription Medications by Outpatients, *Drug Intelligence & Clin. Pharm.* 3:270-7, 196

TEST	HYPOTHYROID	SYNTHROID THERAPEUTIC NORMAL
P.B.I.	Less than 4 mcg %	6-10 mcg %
T_4 By Column	Less than 3 mcg %	7-9 mcg %
T_3 (Resin)	Less than 25%	27-35%
T_3 (Red Cell)	Less than 11%	11.5-18%
Free Thyroxine	Less than 0.7 nanograms %	0.7-2.5 nanograms %
Murphy-Pattee	Less than 2.9 mcg %	4-11 mcg %

Choose the Smooth Road ...to thyroid replacement therapy







HY DOES SYNTHROID OST LESS THAN YNTHETIC DRUGS ONTAINING T_3?

ry simple. T_3 costs more to make nthetically than does T_4. So it is onomically necessary for a nthetic thyroid medication ntaining T_3 to cost more than e containing T_4 alone. Synthetic mbinations cost patients nearly % more than SYNTHROID[3] ecause the T_3 costs more to start ith; also there is the additional xpense of formulating a tablet ntaining two active ingredients.

American Druggist BLUEBOOK, March, 1971.

KNOWLEDGE OF THE '70's CHALLENGES CUSTOMS CONCERNING DESICCATED THYROID DRUGS.

In the past, desiccated thyroid produced from animal glands was considered "good, and cheap." We now know that improved products are available and the price difference has narrowed to the point of being inconsequential. (SYNTHROID, for instance, costs patients about a penny a day more than brands of desiccated thyroid.)

What does this additional $3.65 a year buy the patient? Quite a bit in terms of quality, reliability and service.

SWITCHING PATIENTS TO SYNTHROID IS EASY.

Switching present patients to SYNTHROID (or starting new ones) is a simple matter. SYNTHROID is available in the widest range of dosage strengths of any thyroid drug. Seven scored, color-coded tablet strengths are available plus a lyophilized injectable form for emergency or postoperative uses.

RESPONSE, RELIABILITY, SERVICE—COMPARISON OF FIVE PARAMETERS

PARAMETERS	DESICCATED THYROID U.S.P.	SYNTHROID® (sodium levothyroxine)
SOURCE OF HORMONE	Animal glands (swine, sheep, cows). Hormone content of glands and ratio of T_3-T_4 varies by type of animal, season in which gland is harvested, and diet of animal.[1,2,3,4,5]	Synthetically derived pure crystalline hormone. Because no animal protein is present, no objectionable odor occurs upon aging.
GENERAL ASSAY TECHNIQUE	"Its major disadvantage is inadequate standardization of hormonal content."[8]	Unlike desiccated thyroid U.S.P., thyroxine does not require biologic standardization to establish its potency.[2,6] Crystalline T_4 is used. Purity is verified by paper chromatography. Content of tablets is standardized by weight.
CLINICAL RESPONSE	"T_3 and T_4 ratio varies according to gland source. Fluctuations in response can occur. Potency can vary."[3]	"Sodium levothyroxine has been extensively used with satisfaction and is widely held to be superior to (desiccated) thyroid."[7] "There are well documented examples of patients who failed to respond satisfactorily to desiccated thyroid but subsequently responded to (sodium-l) thyroxine."[4]
PREDICTABILITY	Failure of thyroid U.S.P. treated patients to show clinical improvement and/or lack of correlation in clinical findings to thyroid function test results has been frequently discussed in the literature.[8,9,10,11,12,13,14,15,16] Regardless of which factor or factors accounts for this phenomenon the fact remains that discrepancies do occur.	Test results predictably elevated. ". . . oral potency of this material is attested to by a uniformly good clinical response corroborated by a prompt and sustained increase in the serum PBI levels."[16]

1 Mangieri, C. N. and Lund, M. H.: Potency of United States Pharmacopeia desiccated thyroid tablets as determined by the antigoitrogenic assay in rats. J. Clin. Endocrinol. Metab., *30*:102-4, 1970.
2. Lavietes, P. H. and Epstein, F. H.: Thyroid therapy of myxedema: a comparison of various agents with a note on the composition of thyroid secretion in man. Ann. Intern. Med., *60*:79-87, 1964.
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7 Goodman, L. S. and Gilman, A.: The Pharmacological Basis of Therapeutics, 4th Ed. p. 1479, New York: Macmillan, 1970.
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9. Braverman, L. E. and Ingbar, S. H.: Anomalous effects of certain preparations of desiccated thyroid on serum protein-bound iodine, New Eng. J. Med., *270*:439-42, 1964.
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13. Runyan, J. W.: Hypothyroidism and myxedema, J. Tenn. State Med. Assn., *56*:391-4, 1963.
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15. Catz, B.: Ginsburg, E. and Salenger, S.: Clinically inactive thyroid U.S.P.: a preliminary report, New Eng. J. Med., *266*:136-7, 1962.
16. Bartuska, D. G., et al.: Desiccated thyroid U.S.P. or sodium l-thyroxine?, J. Amer. Med. Women's Assn., *21*:137-9, 1966.

See next pages for prescribing information.







PATIENTS CAN BE SUCCESSFULLY MAINTAINED ON A DRUG CONTAINING THYROXINE ALONE.

Thyroxine (T_4) is, as you know, the major circulating hormone produced by the thyroid gland. T_3 is also produced, in smaller amounts, and is active at the cellular level. For years it has been a working hypothesis among endocrinologists that T_4 is converted by the body to T_3. In 1970 this process, called "deiodination," was demonstrated by Braverman, Ingbar, and Sterling[2]. T_4 does convert to T_3, though the precise quantities are still being studied.

The conversion has been clinically demonstrated during the administration of T_4 to athyrotic patients. Their thyroid status is normalized on SYNTHROID alone, yet the presence of T_3 in these patients has been clearly shown.

CONSIDERATE LONG-TERM THERAPY FOR THE PATIENT.

Predictable patient response, of course, is more important than price. You do get complete clinical response with the single-entity synthetic, SYNTHROID. And, at a reasonable cost to the patient. In some short term situations, T_3 drugs can be useful but, in long term therapy, the smooth road provided by SYNTHROID may be the better route.

SYNTHROID, with its smooth road to complete thyroid replacement therapy, has been selected for more patients in the United States and Canada than any other brand of thyroid medication.

2. Braverman, L. E., Ingbar, S. H., and Sterling, K.: Conversion of Thyroxine (T4) to Triiodothyronine (T3) in Athyreotic Human Subjects, *J. Clin. Invest.* **49**:855-64, 1970.

AS WITH ANY THYROID PREPARATION, CAUTIOUS OBSERVATION OF THE PATIENT DURING THE BEGINNING OF THERAPY WILL ALERT THE PHYSICIAN TO ANY UNTOWARD EFFECTS.

Side effects, when they do occur, are related to excessive dosage. Caution should be exercised in administering the drug to patients with cardiovascular disease. Read the accompanying prescribing information for additional data or write Flint Laboratories.

Choose the Smooth Road ...to thyroid replacement therapy



0.05 mg. 0.1 mg. 0.15 mg. 0.2 mg.

FREE TAB-MINDER medication dispensers—color-coded in 4 dosage strengths—get patients off to a good start and encourage regular habit patterns. Contain free 4-weeks' supply of SYNTHROID and are reusable for maintenance dosage.

APPROXIMATE DOSAGE EQUIVALENTS*

			Animal Gland		
CYTOMEL (Sodium liothyronine) Synthetic T_3	EUTHROID** (Liotrix) Synthetic T_3-T_4	THYROLAR*** (Liotrix) Synthetic T_3-T_4	Desiccated (Thyroid, USP) Cow, sheep or hog thyroid	PROLOID (thyroglobulin) Frozen hog thyroid	SYNTHROID (Sodium levothyroxine) Synthetic T_4
Unscored 5 mcg.	N.A.	N.A.	unscored ¼ gr.	¼ gr.	0.025 mg.
N.A.	½	½	unscored ½ gr.	½ gr.	0.05 mg.
25 mcg.	1	1	unscored 1 gr.	1 gr.	0.1 mg.
N.A.	N.A.	N.A.	N.A.	1½ gr.	0.15 mg.
50 mcg.	2	2	unscored 2 gr.	2 gr.	0.2 mg.
N.A.	3	3	unscored 3 gr.	3 gr.	0.3 mg.
N.A.	N.A.	N.A.	unscored 5 gr.	5 gr.	0.5 mg.
N.A.	N.A.	N.A.	N.A.	N.A.	Injectable 500 mcg.

N.A. = Not Available Commercially

*Equivalents shown are chemical, and do not take into consideration individual patient variables. Clinical effect is approximate and should be monitored when converting a patient to SYNTHROID. This is particularly important in patients previously on desiccated thyroid. In these patients, lower doses of SYNTHROID may produce the same metabolic effect.

**Euthroid (#1 tablet) contains 60 mcg. of T_4 and 15 mcg. of T_3.

***Thyrolar (#1 tablet) contains 50 mcg. of T_4 and 12.5 mcg. of T_3.

Synthroid®
(sodium levothyroxine)



Indications: SYNTHROID (sodium levothyroxine) is specific replacement therapy for diminished o absent thyroid function resulting from primary or secondary atrophy of the gland, congenital de fect, surgery, excessive radiation, or antithyroid drugs. Indications for SYNTHROID (sodium levo thyroxine) **Tablets** include myxedema, hypothyroidism without myxedema, hypothyroidism in preg nancy, pediatric and geriatric hypothyroidism, hypopituitary hypothyroidism, simple (nontoxic goiter, and reproductive disorders associated with hypothyroidism. SYNTHROID (sodium levo thyroxine) **for Injection** is indicated for intravenous use in myxedematous coma and other thyroi dysfunctions where rapid replacement of the hormone is required. The injection is also indicate for intramuscular use in cases where the oral route is suspect or contraindicated due to existin conditions or to absorption defects, and when a rapid onset of effect is not desired.

Precautions: As with other thyroid preparations, an overdosage may cause diarrhea or cramps nervousness, tremors, tachycardia, vomiting and continued weight loss. These effects may begi after four or five days or may not become apparent for one to three weeks. Patients receiving th drug should be observed closely for signs of thyrotoxicosis. If indications of overdosage appear discontinue medication for 2-6 days, then resume at a lower dosage level. In patients with diabete mellitus, careful observations should be made for changes in insulin or other antidiabetic drug dosage requirements. If hypothyroidism is accompanied by adrenal insufficiency, as Addison's Dis ease (chronic subcortical insufficiency), Simmonds's Disease (panhypopituitarism) or Cushing' syndrome (hyperadrenalism), these dysfunctions must be corrected prior to and during SYNTHROI (sodium levothyroxine) administration. The drug should be administered with caution to patient with cardiovascular disease; development of chest pains or other aggravations of cardiovascula disease requires a reduction in dosage.

Contraindications: Thyrotoxicosis, acute myocardial infarction. **Side effects:** The effects of SYN THROID (sodium levothyroxine) therapy are slow in being manifested. Side effects, when they d occur, are secondary to increased rates of body metabolism; sweating, heart palpitations with o without pain, leg cramps, and weight loss. Diarrhea, vomiting, and nervousness have also beer observed. Myxedematous patients with heart disease have died from abrupt increases in dosage o thyroid drugs. Careful observation of the patient during the beginning of any thyroid therapy wil alert the physician to any untoward effects.

In most cases with side effects, a reduction of dosage followed by a more gradual adjustment upward will result in a more accurate indication of the patient's dosage requirements without the appearance of side effects.

Dosage and Administration: The activity of a 0.1 mg. SYNTHROID (sodium levothyroxine) TABLE is equivalent to approximately one grain thyroid, U.S.P. Administer SYNTHROID tablets as a single daily dose, preferably after breakfast. In hypothyroidism without myxedema, the usual initial adult dose is 0.1 mg. daily, and may be increased by 0.1 mg. every 30 days until proper metabolic balance is attained. Clinical evaluation should be made monthly and PBI measurements about every 90 days. Final maintenance dosage will usually range from 0.2-0.4 mg. daily. In adult myxedema, starting dose should be 0.025 mg. daily. The dose may be increased to 0.05 mg. after two weeks and to 0.1 mg. at the end of a second two weeks. The daily dose may be further increased at two-month intervals by 0.1 mg. until the optimum maintenance dose is reached (0.1-1.0 mg. daily).

Supplied: Tablets: 0.025 mg., 0.05 mg., 0.1 mg., 0.15 mg., 0.2 mg., 0.3 mg., 0.5 mg., scored and color-coded, in bottles of 100, 500, and 1000. Injection: 500 mcg. lyophilized active ingredient and 10 mg. of Mannitol, N.F., in 10 ml. single-dose vial, with 5 ml. vial of Sodium Chloride Injection, U.S.P., as a diluent. SYNTHROID (sodium levothyroxine) **for Injection** may be administered intravenously utilizing 200-400 mcg. of a solution containing 100 mcg. per ml. If significant improvement is not shown the following day, a repeat injection of 100-200 mcg. may be given.

FLINT LABORATORIES
DIVISION OF TRAVENOL LABORATORIES, INC
Morton Grove, Illinois 60053

THE FACTS ARE CLEAR AND HERE IS OUR OFFER.

Synthetic thyroid drugs are an improvement over animal gland products. Patients, even athyrotic ones, can be completely maintained on SYNTHROID (T_4) alone. Thyroid function tests are easy to interpret since they are *predictably* elevated when the patient adheres to SYNTHROID. Of all synthetic thyroid drugs, SYNTHROID is the most economical to the patient.

OFFER: AA
Free TAB-MINDER medication dispensers to start or convert all your hypothyroid patients to SYNTHROID. Free information to physicians on role of thyroid function tests in a new booklet titled: "Guideposts to Thyroid Therapy." Ask us.

Name _____

Address _____

City _____ State _____ Zip _____

Thank You, Doctor



Your continuing cooperation with the American Association of Medical Assistants has been generous. With your support our organization has achieved a membership of 14,000 medical assistants in more than 400 chapters in 45 states, District of Columbia and Puerto Rico.

Since our first organizational meeting 15 years ago, we have worked toward the primary goal of providing educational opportunities to the medical assistant in the doctor's office. In a short decade and a half the association has:

- Established and conducted a certification program as an incentive to self-education.
- Developed curricula for medical assisting programs in hundreds of junior and community colleges.
- Carried on a continuing education program for medical assistants through seminars, workshops and a professional bi-monthly journal.
- Published career materials and established a scholarship loan fund to help recruit future medical assistants.
- Cooperated with AMA in public relations efforts beneficial to the medical profession as a whole.

But our work cannot stop here. As the only national association for medical assistants, AAMA is eager to contribute to advancement of this allied health field. We would like to share our educational programs with all of the medical assistants across the nation. But to do this we need the co-operation of many more physicians.

If your medical assistant is not a member of AAMA, please fill out this coupon today. Her greater knowledge of medical assisting will be your reward.

American Association of Medical Assistants

I wish to inquire about membership for my medical assistant in the American Association of Medical Assistants, Inc. Please have someone send more information to:

Name _____

Business Address _____ Phone _____
(Street)

City _____ State _____ Zip _____

Member of county medical society: Yes _____ No _____

County _____

Name of Assistants:	Address:
_____	_____
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Clip and mail to:

American Association of Medical Assistants
One East Wacker Drive
Chicago, Illinois 60601

P.S. AAMA bylaws provide that the association, "is not, nor shall it ever become a trade union or collective bargaining agency."

Old winner, new bottle.



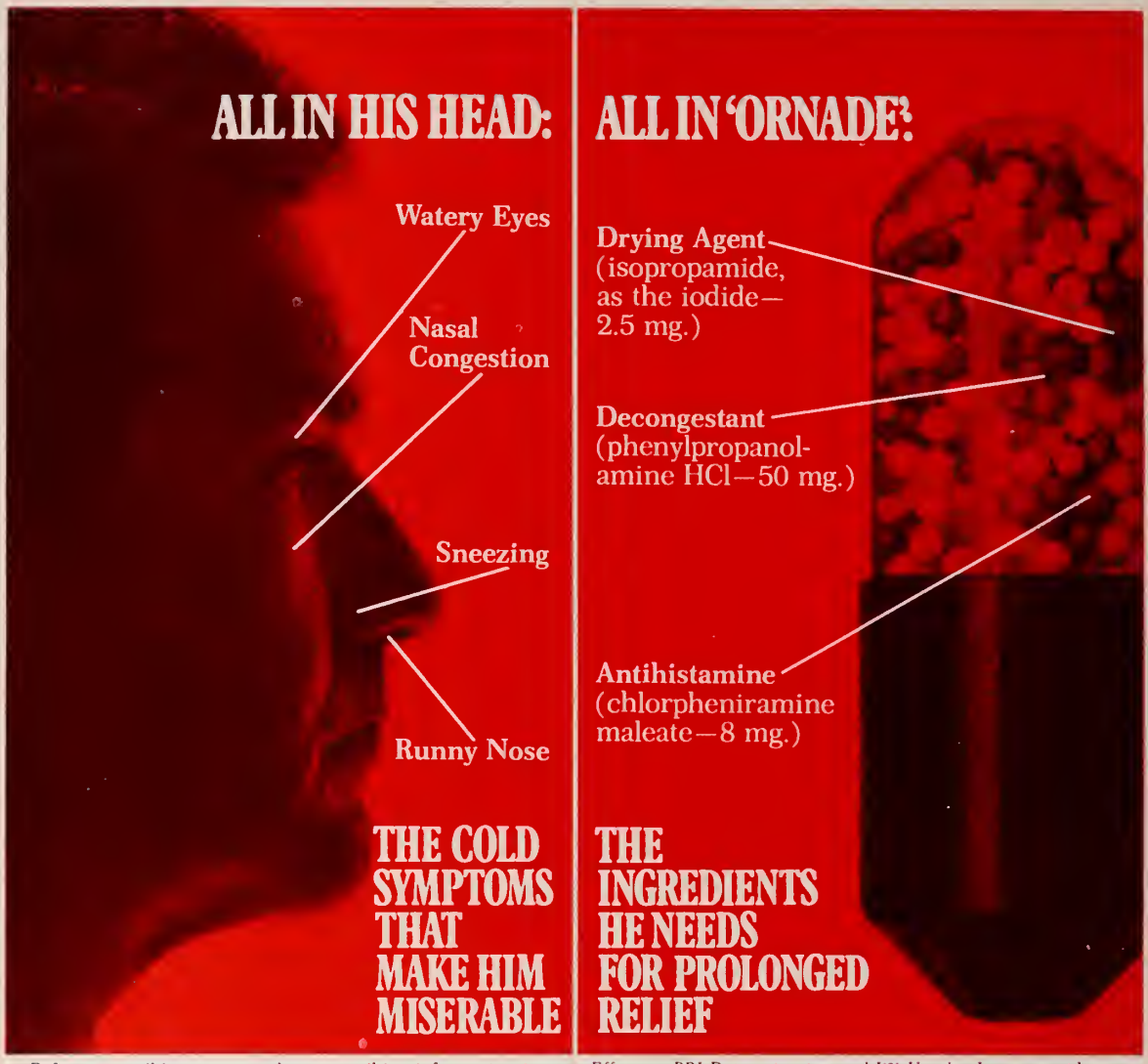
DBI® phenformin HCl tablets of 25 mg.
DBI-TD® phenformin HCl capsules of 50 and 100 mg.

Indications: Stable adult diabetes mellitus; sulfonylurea failures, primary and secondary; adjunct to insulin therapy of unstable diabetes mellitus.
Contraindications: Diabetes mellitus that can be regulated by diet alone; juvenile diabetes mellitus that is uncomplicated and well regulated on insulin; acute complications of diabetes mellitus (metabolic acidosis, coma, infection, gangrene); during or immediately after surgery where insulin is indispensable; severe hepatic disease; renal disease with uremia; cardiovascular collapse (shock); after disease states associated with hypoglycemia.
Warnings: Use during pregnancy is to be avoided.
Precautions: 1. *Starvation Ketosis:* This must be differentiated from "insulin lack" ketosis and is characterized by ketonuria which, in spite of relatively normal blood and urine sugar, may result from excessive phenformin therapy, excessive insulin reduction, or insufficient carbohydrate intake. Adjust insulin dosage, lower phenformin dosage, or supply carbohydrates to alleviate this state. **Do not give insulin without first checking blood and urine sugar.**
2. *Lactic Acidosis:* This drug is not recommended in the presence of azotemia or in any clinical situation that predisposes to sustained hypotension that could lead to lactic acidosis. To differentiate lactic acidosis from ketoacidosis, periodic determinations of ketones in the blood and urine should be made in diabetics previously stabilized on phenformin, or phenformin and insulin, who have become unstable. If electrolyte imbalance is suspected, periodic determinations should also be made of electrolytes, pH, and the lactate-pyruvate ratio. The drug should be withdrawn and insulin, when required, and other corrective measures instituted immediately upon the appearance of any metabolic acidosis.
3. *Hypoglycemia:* Although hypoglycemic reactions are rare when phenformin is used alone, every precaution should be observed during the dosage adjustment period particularly when insulin or a sulfonylurea has been given in combination with phenformin.
Adverse Reactions: Principally gastrointestinal; unpleasant metallic taste, continuing to anorexia, nausea and, less frequently, vomiting and diarrhea. Reduce dosage at first sign of these symptoms. In case of vomiting, the drug should be immediately withdrawn. Although rare, urticaria has been reported, as have gastrointestinal symptoms such as anorexia, nausea and vomiting following excessive alcohol intake.
(B)98-146-103-C

For complete details, including dosage, please see full prescribing information.

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardsley, New York 10502
Distributors

DBI-8345-9



Before prescribing, see complete prescribing information in SK&F literature or *PDR*.

Indications: Upper respiratory congestion and hypersecretion associated with: the common cold; acute and chronic sinusitis, vasomotor rhinitis; allergic rhinitis (hay fever, "rose fever," etc.).

Contraindications: Hypersensitivity to any component; concurrent MAO inhibitor therapy; severe hypertension; bronchial asthma; coronary artery disease; stenosing peptic ulcer; pyloroduodenal or bladder neck obstruction. Children under 6.

Warnings: Advise vehicle or machine operators of possible drowsiness. Warn patients of possible additive effects with alcohol and other CNS depressants.

Usage in Pregnancy. In pregnancy, nursing mothers and women who might bear children, weigh potential benefits against hazards. Inhibition of lactation may occur.

Effect on PBI Determination and I^{131} Uptake: Isopropamide iodide may alter PBI test results and will suppress I^{131} uptake. Substitute thyroid tests unaffected by exogenous iodides.

Precautions: Use cautiously in persons with cardiovascular disease, glaucoma, prostatic hypertrophy, hyperthyroidism.

Adverse Reactions: Drowsiness, excessive dryness of nose, throat or mouth; nervousness; or insomnia. Also, nausea, vomiting, epigastric distress, diarrhea, rash, dizziness, weakness, chest tightness, angina pain, abdominal pain, irritability, palpitation, headache, incoordination, tremor, dysuria, difficulty in urination, thrombocytopenia, leukopenia, convulsions, hypertension, hypotension, anorexia, constipation, visual disturbances, iodine toxicity (acne, parotitis).

Supplied: Bottles of 50 capsules.

SK&F *Smith Kline & French Laboratories*

Trademark

ORNADE® SPANSULE®

brand of sustained release capsules

Each capsule contains 8 mg. of Teldrin®(brand of chlorpheniramine maleate), 50 mg. of phenylpropanolamine hydrochloride; 2.5 mg. of isopropamide, as the iodide.

UNCOMMON RELIEF FOR COLD SYMPTOMS

OR-203

a winner in the tetracycline "500"



TETRACYN® 500
(TETRACYCLINE HCl, 500-mg capsules)
GETS POINTS FOR LOW COST... SCORES HIGH IN CONVENIENCE

ROERIG Pfizer

A division of Pfizer Pharmaceuticals
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Call it what you will, it may be premalignant.

Before

3/29/67 Before therapy with 5%-FU cream. Patient P. T. shows a moderately severe solar keratotic involvement. Note residual scarring from the previous cryosurgical and electrosurgical procedures on forehead and ridge of nose adjacent to periauricular area.

After

6/12/67 Seven weeks after cessation of therapy. Reactions have subsided. Residual scarring is not seen except for that due to prior surgery. Inflammation has disappeared and face is clear of keratotic lesions.



ROCHE
Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

and Efudex® (fluorouracil) 5% cream can resolve it.

Call it actinic, solar or senile keratoses, many regard it as "precancerous."[1,2]

Topical fluorouracil, considered by some dermatologists to be a major advance in the treatment of multiple solar keratoses,[3,4] offers the physician a relatively inexpensive alternative to cryosurgery, electrodesiccation and cold knife surgery. Of the topical fluorouracils available, only Efudex offers 2% and 5% solution and 5% cream formulations—formulations that have proved effective in the treatment of these mutliple lesions.

Usual duration of therapy, 2 to 4 weeks.

Studies showed that with the 2% and 5% Efudex preparations, the usual duration of therapy was only 2 to 4 weeks.[5] Other studies with topical fluorouracil revealed that when concentrations of less than 2% were used, significant numbers of lesions recurred.[6]

Treats the lesions you can't see, too.

Numerous lesions, not apparent prior to 2% and 5% Efudex therapy, manifested themselves by definite reactions, while intervening skin remained relatively unaffected.[5] The early eradication of these subclinical lesions (which may otherwise have undergone further progression) probably accounts for the reduced incidence of future solar keratoses in patients treated with topical fluorouracil—especially with 5% concentrations.[6]

How to identify solar keratoses.

Typically, the lesion—a flat or slightly elevated brown to red-brown papule—is dry, rough, adherent and sharply defined. Multiple lesions are the rule.

Predictable therapeutic response.

The response to a typical course of Efudex therapy is usually characteristic and predictable. After 3 or 4 days of treatment, erythema begins to appear in the area of keratoses. This is followed by a moderate to intense inflammatory response, scaling and occasionally moderate tenderness or pain. The height of this response generally occurs two weeks after the start of therapy and then begins to subside as treatment is stopped. Within two weeks of discontinuing medication, the inflammation is usually gone. Lesions that do not respond should be biopsied.

References: 1. Allen, A. C.: *The Skin, A Clinicopathological Treatise*, ed. 2, New York, Grune & Stratton, 1967, p. 842. 2. Dillaha, C. J.; Jansen, G. T, and Honeycutt, W. M.: "Treatment of Actinic Keratoses with Topical Fluorouracil," in Waisman, M. (ed.): *Pharmaceutical Therapeutics in Dermatology*, Springfield, Ill., Charles C Thomas, 1968, p. 92. 3. Belisario, J. C.: *Cutis, 6*:293, 1970. 4. Sams, W. M.: *Arch. Derm., 97*:14, 1968. 5. Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey. 6. Williams, A. C., and Klein, E.: *Cancer, 25*:450, 1970.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

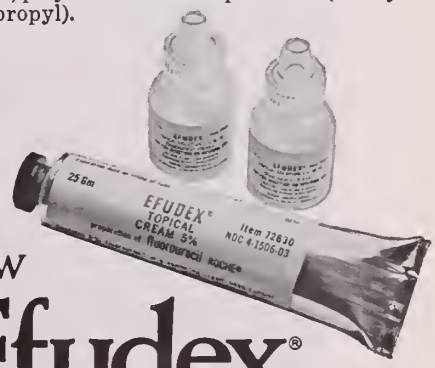
Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

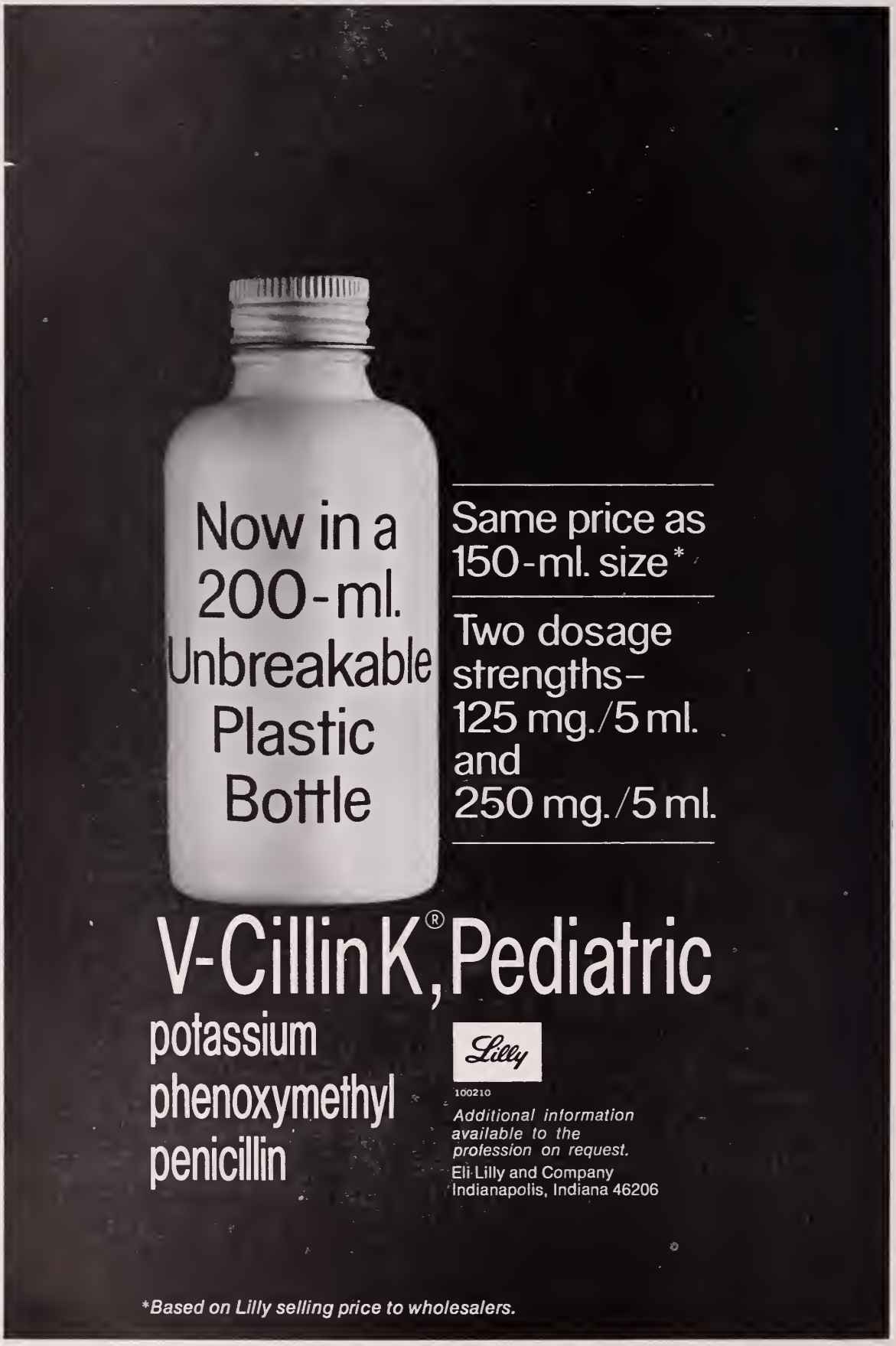
Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).



now
Efudex®
(fluorouracil)
cream/solution


Now in a 200-ml. Unbreakable Plastic Bottle
Same price as 150-ml. size*
Two dosage strengths– 125 mg./5 ml. and 250 mg./5 ml.
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*Based on Lilly selling price to wholesalers.

I Doubt It

SINCE READING Dr. "Pete" Riley's excellent article (beginning on page 107) about penicillin, I have been haunted by a question: If the FDA had been in existence in the late nineteen thirties and functioning the way it does today, would we now have penicillin?

The question haunts me because I can not arrive at a definite answer. I don't know, for sure, how the FDA operates today. I don't know what factors it considers of paramount significance in the evaluation of new drugs. I don't know whose judgment prevails and I don't know the basis of that judgment.

Perhaps the organization and operational policies of the FDA allow for the expeditious processing and disposition of certain drug application. I doubt it.

Perhaps the primary objective of the FDA is to increase the number of effective drugs available to physicians engaged in the practice of medicine and the treatment of patients stricken with disease. I doubt it.

Perhaps the authority of the FDA derives from the public whose welfare it alleges to promote and protect. I doubt it.

Perhaps the decisions of the FDA represent a concensus of expert pharmacologists, toxicologists, pathologists and medical practitioners, expressed openly, developed in concert and weighted equally. I doubt it.

Perhaps the actions taken by the FDA reflect confidence in the training, experience and wisdom of the practicing physician. Maybe the experts of the FDA even seek the opinions of physicians and respect their judgment. I doubt it.

Perhaps the men and women who make the decisions of the FDA are willing to assume personal liability for the effects and results of those decision, as practicing physicians must for their decisions. I doubt it.

Perhaps the FDA will, ultimately, promote drug research and development instead of discouraging it as is now the case; lower the costs of drugs rather than raise them as is now the case; assist physicians and pharmacists in their tasks instead of frustrating them as is now the case; strengthen the bonds of trust between patients and physicians rather than destroying it as is now the case; function as a source of scientific knowledge and advice for a nation of people instead of a pedantic and dictatorial tool for a bureaucracy with largely political objectives, as is now the case. Perhaps, but I doubt it.

So the question continues to haunt me: Would we have penicillin . . . or digitalis, morphine, aspirin, smallpox vaccine, x ray machines, ether or quinine . . . if their original use had been subject to the prevailing requirements, rules and regulations of the FDA? It is a much more complex question than it appears, and finding the answer is much more difficult.

Can anyone know how much he suffers because an imperfect wisdom condemned the source of his relief? Can the patient who died of cancer yesterday be grateful that he was not subjected to the hazards of a cure, unprocessed and unapproved by the FDA?—

I doubt it. *MRJ* □



In addition to attendance at State Society Committee functions, your president meets with other organizations having medical affiliation or interests. Participation may be as an active member, consultant, observer or guest. Two organizations warrant special mention, the Department of Institutions, Social and Rehabilitative Services and the Oklahoma Regional Medical Program. Both involve countless hours of meeting time, are concerned with patient welfare, employ state and federal funds and include lay and medical membership.

Other than the knowledge that these organizations exist, how much and what do we know about them? I confess that, prior to my involvement, my understanding was minimal and my concern perhaps even less. In the past few months however, I have been in a position as participant and able to appreciate the problems and the dedication manifested by the members.

The director of the Department of Institutions, Social and Rehabilitative Services, L. E. Rader, is well known to us as an able administrator with a genuine concern for both the physician provider and patient beneficiary. His Advisory Committee on Medical Care for Public Assistance Recipients is chaired by Walter Brown, MD, one of our physicians and sharing its deliberations are representatives of all allied health agencies. Though some of the meetings are of long duration, I feel that the general tenor is one of sincerity, concern and honesty. Many in our profession may justifiably take issue with policy matters and disagree with solutions, but one must note that direction is supplied by federal fiat and funding. One might ask, "Is it the state organization which may become the vehicle for federalization of medicine?"

The Core Director of the Oklahoma Regional Medical Program is Dale Groom, MD. Mark R. Johnson, MD, has recently completed his term as Chairman of the Regional Medical Advisory Group (RAG). Both have to be congratulated for outstanding accomplishments during the four years existence of the program. C. Riley Strong, MD, also chairman of our Board of Trustees, has succeeded Doctor Mark Johnson. A bright future is predicted in the development and fruition of projects for delivery of medical care and spread of medical knowledge throughout the state. This totally federally funded program receives maximum work and effort for the funds supplied because democratic interested people, including health professionals and consumers, are involved. Though operating under a financial handicap, it is hoped that adequate funds for the many worthwhile projects programmed for this year will be forthcoming.

Anyone without a detailed narrative of the objectives, philosophy, operations and attainments of these two organizations is apt to be suspicious and skeptical. I submit however that in the light of my present experience, both deserve the well-wishes and cooperation of our society members. □

Sincerely,

Lucien H. Pascuzzi

OSMA JOURNAL/scientific

Thrombosis, A Review

JAMES P. RHOADS, MD

Wherein the normal mechanism of hemostasis and the pathologic condition of thrombosis are examined and contrasted.

IN THE WELL human being, there are several contributors to normal hemostasis. These include plasma, blood cells, the nervous system and the vessel wall. Damaged or cut blood vessels contract, but this alone is insufficient to arrest hemorrhage and this is not the entire role played. Subendothelial collagen and the basement membrane, when exposed, come in contact with platelets and trigger the hemostatic process. The vessel wall also provides thromboplastin, a particulate intracellular lipoprotein which is released by cellular injury and triggers the extrinsic clotting system, both in the plasma and probably also on the platelet surface. Within seconds of injury to a vessel, platelets are observed to adhere to the area of trauma. More platelets soon begin to arrive from the general circulation and stick to those initially deposited. The abnormal opening in the vessel wall becomes progressively occluded by a platelet mass known as a hemostatic platelet plug. The platelet plug does not form inside the vessel where the endothelium is intact but as a capsule around the opening of the severed vessel. At first the plug is slightly permeable and small amounts of blood can be seen to escape. Within a short time, however, it becomes impermeable and the opening is sealed. The plug is now said to be consolidated.

During this time, the blood coagulation process has also been activated, and fibrin deposition is already in evidence, especially at the periphery of the hemostatic plug. This activation can occur through the extrinsic plasma clotting system being triggered by tissue thromboplastin released from the vessel wall or surrounding tissues as mentioned above, or through the triggering of the intrinsic system. How this latter occurs is not known, but it may be related to substances made available from the platelets in association with platelet factor three. The coagulation of plasma with fibrin formation which reinforces and seals the platelet plug is the last event in primary hemostasis. It is important to note that the initial phases of vasoconstriction and platelet accumulation can take place normally in anticoagulated subjects and in patients or animals with coagulation disorders.

Finally, the damaged vessel is repaired. The formation of fibrin is important in wound healing because it serves as a substrate for fibroblasts which produce fibers

and ground substance for normal repair.

Welch in 1899 complained about "the old and still common conception that a thrombus was essentially a blood coagulum." It continues to be important to draw the distinction between a blood clot and a thrombus.

A blood clot is a structure formed in static blood in a container in the laboratory and consisting of red cells, white cells, and platelets randomly dispersed in a fibrin network. A thrombus, on the other hand, is formed in moving blood and is composed of a head and a tail. The head consists of masses of agglutinated platelets with numerous white cells but very few red cells and only a small amount of fibrin. The tail consists of fibrin containing entrapped red cells. In an arterial thrombus, the major component is usually the platelet head. In the venous system the platelet head may be quite small where it is attached to the vessel wall, with a much larger red tail streaming away in the direction of the blood flow. Indeed, as stated in a recent editorial by Doctor Sherry, ". . . still a matter of controversy in the pathogenesis of venous thrombosis is whether the activation of the clotting mechanism is carried out through an independent mechanism or follows the formation of a small platelet nidus; the latter would suggest some commonness with the pathogenesis of its arterial counterpart."

A platelet head and fibrin tail are common to the structure of both a hemostatic plug and a thrombus. It seems likely then that the process of thrombosis is the same as that of hemostatis, but is applied misappropriately.

It is very important to remember that arterial thrombosis results, in most cases, from the formation of a large exuberant platelet mass at the site of a definite vascular injury. This is the critical step in the formation of an arterial thrombus.

Such an arterial thrombus begins with local accumulation of platelets, some of which are adherent to the wall. More platelets then aggregate at the site to form, at first, a predominantly platelet mass. This may give rise to multiple small emboli or continue to build until it has some effect on the local blood flow. When this occurs, platelets at the periphery of the mass undergo morphological changes, so called viscous metamorphosis. It is at this juncture that leukocytes begin to adhere to the platelets and polymerized fibrin is seen in significant amounts for the first time. Small mural thrombi may not advance beyond this stage. When stagnant columns or pockets of blood are created, further coagulation may occur as a secondary event and this adds to the total bulk of the mass. Vessel occlusion may occur.

As time passes, there is an increase in the proportion of fibrin to platelet material so that the latter may appear to undergo a fibrinous transformation. The number of leukocytes also increases to be followed by autolytic and degenerative changes and the eventual organization of any unresolved material that remains.

Because of the important role that platelets play in thrombosis, particularly arterial thrombosis, we will now consider their function further. Subsequent to vessel injury, the first thing that is done by platelets is adherence at the site of injury. Young platelets adhere to collagen more readily than do older platelets. Electronmicroscopy has led to the general recognization that the initial platelet layer does not attach to damaged endothelial cells, but rather to newly exposed collagen fibers in the connective tissue beneath the damaged endothelium. The platelet-collagen interaction has been shown to be a specific biochemical phenomenon. It requires the presence of free amino groups, especially the epsilon amino group of lysine. The platelet-collagen reaction resulting in adhesion of platelets to the collagen does not require any cofactors. This platelet-collagen contact then results in important biochemical and morphologic changes in the platelets. This is termed the secretory phase of platelet function and is characterized by release or surface exposure of certain platelet substances. The intracellular platelet granules disappear and ADP, serotonin, and other platelet components appear in the surrounding medium. This release is dependent upon divalent cations, particularly calcium, and upon a source of metabolic energy. Platelet metabolism uses glucose as its primary energy source and may proceed through either oxidative or anaerobic pathways.

Adsorbed on the platelet surface are significant amounts of plasma coagulation factors 1, 5, and 11, as well as lesser amounts of several other factors. As a result of the secretory phase of platelet activity, there also appears on the surface a lipoprotein known as platelet factor 3, which is essential for the proper function of the intrinsic clotting system. In vivo, the platelet factor 3 activity appears before the formation of thrombin is detectable. In truth, the term platelet factor 3 is misleading, since there is no single such factor. It actually designates an activity unique to platelets and not a biochemical entity that can be isolated.

It has been shown that platelets exposed to glass are capable of clotting hemophiliac plasma. Since the intrinsic system is defective in such patients, coagulation must take place through the extrinsic pathway of prothrombin activation. It has been proposed that platelets provide a substance distinct from platelet factor 3, since platelet factor 3 has no effect on the extrinsic system. Platelets, by various manipulations, can be induced to develop tissue-factor-like activity. Such platelets promote clotting by way of the extrinsic system.

The secretory phase of platelet activity also makes available platelet factor 4, a specific protein antiheparin. Platelet factor 4 possibly also promotes reversible aggregation of platelets and precipitates fibrinogen-fibrin intermediates. The serotonin that is released during the secretory phase is a vascular constrictor. Epinephrine is also released and acts to promote platelet aggregation.

However, probably the most important substance released during the secretory phase, in regard to subsequent stages of platelet function, is ADP. This promotes aggregation and cohesion of new platelets arriving from the blood stream and initiates the next stage in platelet function; that is the formation of reversible platelet aggregates. It has also been proposed that additional ADP may be available from damaged cells in the vascular wall. Since the ADP molecule is unable to traverse the platelet membrane, its effect is assumed to occur at the cell surface, but the precise mode of action is still under study. Fibrinogen and at least one other plasma cofactor, as well as sources of metabolic energy, are required for ADP induced platelet aggregation. Electronmicroscopy of this phase has shown that the plasma membranes of the aggregated platelets remain intact. This aggregation of platelets is reversible but the reason for the reversibility is not known. However, platelets will de-aggregate after the passage of time even if relatively large amounts of ADP are still present in the medium. Unlike the case in adherence to collagen, platelet age does not affect ADP aggregation. The life span of a platelet is eight days.

Platelets have two distinct adenine nucleotide pools. One of these is metabolically inert and available for release by the action of collagen and the other is not released by collagen but remains in the platelet to participate in cellular nucleotide metabolism.

Platelets in the circulation are morphologically thin and disk-like, with a volume of about 5.8 cubic microns. Aggregation by ADP is immediately preceded by a change in shape from a disk to a "spiny sphere." This alteration is invariably accompanied by an increase of at least 15 percent in platelet volume. Inhibitors of aggregation also prevent the change in shape. The epinephrine induced aggregation response is unique in that platelets aggregate without changing shape.

The next stage of platelet function is that of irreversible aggregation. It is caused by the presence of thrombin, which is presumably formed on the platelet surface by clotting factors adsorbed from the plasma. Thrombin causes complete release of platelet factors and contraction of the entire platelet aggregate. This latter effect probably is mediated by the contractile protein thrombasthenin. At this stage the plug becomes impermeable. Newly arrived platelets are rapidly clumped and degranulated in the presence of thrombin. The sum of

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these responses to thrombin is known as "viscous metamorphosis." The amount of thrombin required for this is less than that needed to polymerize fibrinogen. The agglutinating action of thrombin operates through the ADP mechanism and indeed ADP and thrombin seem to have a synergistic effect in aggregating platelets.

As more thrombin is formed, it also operates on its main substrate, plasma fibrinogen, which is converted to additional fibrin. At this point in time, microscopic fibrin strands can be seen at the periphery and these soon become the most important components of the plug. If insufficient fibrin is present, the plug will be unstable and a "rebleeding phenomenon" will occur. In a matter of hours to days, almost all the platelets are replaced by fibrin, which now become the principal support of the plug. In its final stages, the plug is invaded by mononuclear cells and there is evidence of phagocytosis of the platelets and fibrin.

We now come to the point where we must examine the relationship between thrombosis and atheromatous plaques. The lesions of atherosclerosis have a focal distribution in the tunica intima of the aorta and larger distributing arteries. These consist of raised plaques, containing rather widely differing amounts of fibrous and fatty material and other degenerate debris. In general, these lesions produce clinical effects only when they encroach significantly on the lumen of the artery and thereby cause tissue ischemia in its territory of supply.

Although the exact mechanism of atherogenesis is unknown, several theories have been proposed that have merit:

1. The filtration hypothesis. This ascribes the development of the lesions to the retention within the intima of lipids and other plasma constituents which enter the wall from the arterial lumen.

2. Injurious mechanical factors acting inside the arterial wall.

3. Metabolic disturbances within the arterial wall.

4. Incorporation within the intima of materials which formed as a surface deposit from the blood. This is known as the encrustation theory or thrombogenic hypothesis.

The encrustation theory was first proposed by Carl Rokitansky in 1842. It was supported by the laminated character of some plaques and the presence of fibrin within them. Duguid, in the late 1940's, demonstrated that if a mural thrombus forms on the surface of any artery and persists, it will be covered by new epithelium, to become in effect a thickened part of the intima. If the process is repeated, successive strata of the incorporated material will significantly reduce the lumen of the artery. Having been incorporated in this way, the thrombus material will undergo degenerative changes and cellular organization which tends to obscure its origin. Finally it will be no longer distinguishable from the necrotic debris which is often characteristic of the more advanced atherosclerotic lesions.

To quote from the late Doctor French, ". . . while there is good evidence that occluding thrombi occur as a complication in the advanced stage of atherosclerosis and lead to ischemia and infarction, and reasonably good evidence that mural thrombi also occur as a complication which can be clinically silent but lead to growth of the plaques, the view that the lesions can begin or progress from an early stage in this way has to be based, at present, more on plausibility than established fact."

No matter how the plaques begin, an occluding arterial thrombus in association with the plaque is very often the significant event leading to tissue infarction and clinical disease. Why does the occluding thrombus form?

Frequently the vessel lumen is already narrowed, often to as much as one-third its original diameter. This causes disturbed blood flow with zones of high velocity gradient, turbulence, and eddy currents. These may favor platelet accumulation. The more immediate stimulus is now believed to be a break in the lining membrane of the vessel through the rupture or ulceration of a necrotic portion of the arteriosclerotic lesion in the wall. Frequently such breaks are associated with evidence of hemorrhage into the wall, but the question remains, did the hemorrhage precede the break or result from it?

However, the thrombus need not occlude the vessel to cause disease. Because blood continues to flow past the free surface of a mural thrombus, it is a potential source of multiple small emboli which can be carried further on into the same arterial tree. It is now well established that mural thrombi in the internal carotid arteries can have secondary effects on the cerebral circulation in this way.

Small emboli which lodge in the retinal vessels can be viewed directly and their presence related to transient attacks of retinal ischemia. The same process may operate in other vascular beds and is now thought to be involved in some cases where myocardial ischemia is not associated with a detectable occluding thrombus. This has received some experimental support from studies where ADP has been infused in the coronary circulation of swine. Multiple platelet aggregates develop in the microcirculation leading to microscopic and gross evidence of myocardial infarction in those animals surviving the infusion for two hours or more.

The question now arises, is there such a thing as a hyper-coagulable state and do some of the so-called risk factors in ischemic heart disease and other illnesses associated with atheromatous plaque operate through the thrombotic mechanism? In other words, despite the presence of the plaque it might require some change in the blood, such as increased platelet stickiness or hyper-coagulability to predispose or to trigger the occluding event. Certain disease processes, such as polycythemia, PNH, disorders with an overabundance of platelets, etc., are well known to be associated with an increased risk of thrombosis. However, such clear cut predisposing conditions are not usually found in the people with ischemic heart or cerebral vascular disorders. If hyper-coagulable states exist in these people, they are more subtle.

The theory that there is a hemostatic balance between a continuous deposition of fibrin by coagulation and removal by the fibrinolytic system has much evidence to favor it. There is a plasma inhibitor for each activated stage in the coagulation mechanism. Certainly subtle disorders in this sort of a dynamic system could increase the likelihood of coagulation. It is well known that even a moderate congenital deficiency of certain of the antithrombins is associated with a definite thrombotic tendency. Efforts are currently under way to assay coagulation reactant products as biochemical markers of an increased tendency to thrombosis even in apparently well people.

We have seen that it is the platelets that are critically important in thrombosis in the arterial system. Mitchell suggests that, "It may be that in human thrombotic disease the circulating cells are themselves abnormal so that the role of the arteries is simply to furnish flow situations which encourage cell to cell adherence." It has been demonstrated that patients with ischemic heart disease or peripheral vascular disease have increased sensitivity of their platelets to ADP. During the past ten years, it has become apparent that environmental factors may influence platelet function. For instance, it is known that tobacco usage increases blood epinephrine levels and we have seen that epinephrine is a promoter of platelet aggregation. Diets rich in dairy products in experimental animals have been shown to enhance thrombus formation in extra corporeal shunts. Also animals fed diets rich in saturated fats were found to have a higher incidence of ADP induced aggregates in the small vessels following an infusion of ADP than animals fed a normal diet.

The foregoing has therapeutic implications. We can encourage patients to modify certain of the environmental factors, such as tobacco use and diets rich in saturated fats. In venous thrombosis where, regardless of the initiating event, the dominant pathologic feature and critical step is the activation of the coagulation mechanism, anticoagulants are valuable. They appear to be able to prevent venous thrombosis in patients who are at risk, to prevent embolization in patients who have already developed leg vein thrombosis, and to prevent the recurrence of emboli in patients who have already sustained an embolus. We already have, therefore, an antithrombotic agent in respect to the venous system. However, there is no evidence that anticoagulants substantially modify the course of arterial thrombosis. The critical event here is the formation of the platelet mass.

Many agents are known to interfere with platelet function. For instance, the following inhibit platelet aggregation: ATP, AMP, adenosine, prostaglandin E_1, phenothiazines, dipyridamole ("Persantine"),® antihistamines, local anesthetics, heparin, aspirin, phenylbutazone, indomethacin, azathioprine, and dextran. Curiously, the only common denominator of the large group of platelet aggregation inhibitor drugs is the capacity for vasodilatation. It is conjectured that these may somehow affect the platelet contractile protein.

Aspirin inhibits the aggregation of platelets that occurs on exposure to collagen and the so-called secondary phase of in vitro ADP aggregation. Dipyridamole ("Persantine") reduces platelet adhesiveness and first phase aggregation. Preliminary studies suggest that it has no benefit in cerebral vascular and coronary artery disease. However, "Persantine" has been statistically of significance in association with anticoagulants in preventing thrombi on prosthetic valves. It should be also mentioned that aspirin and "Persantine," along with adenosine, prostaglandin E_1, heparin, and cholchicine are inhibitors of the platelet secretory or release reaction.

To date, there are no good studies of aspirin in arterial thrombotic disorders. However, a recent study has shown that aspirin is statistically equivalent in effect to coumadin and low molecular weight dextran in preventing venous thromboembolism following arthroplasty of the hip, a procedure ordinarily with about a 39 percent risk of venous thromboembolism.

It will be of great theoretical and, hopefully, practical interest to learn the outcome of studies now planned or in progress designed to test agents capable of altering normal platelet function. □

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Clinical Notes

B. C. CHATHAM, MD
REX PATY, ASMT

In view of epidemic incidence of gonorrhea the authors cultured all private patients of B.C.C. for a specified period of time finding one positive culture. The authors feel this is a select group of women and the results do not reflect the true incidence of gonorrhea in the general population.

DURING RECENT YEARS much publicity in both professional literature and lay press has emphasized the high incidence—even in epidemic proportions—of gonorrhea in the population. Also much stress has been put on the fact that infected persons have not been treated. Even more emphasis has been placed on the disease's prevalence in the teenage population.

After discussing these facts the authors decided to run an experiment on the segment of population seen by the senior author. We decided to do rectal and cervical cultures on all women on whom the author did pelvic exams during a period of two weeks. No patient was excluded from this except those postoperative patients who had no cervix. Finally no patient was aware of the tests made and no charges were made.

THE TECHNIQUE

1. We used commercially available Martin-Lester[1] media in 30 cc bottles containing carbon dioxide and with media slanted for easy innoculation.

2. With the patient in dorsal lithotomy position a clean dry Graves speculum was inserted in the vagina and the culture taken from the endocervix with a sterile swab, and immediately streaked on media, held upright to retain carbon dioxide.

3. Using a sterile swab a specimen was taken from the rectum and placed on media in the same manner.

4. The specimen bottles were then taken immediately to the laboratory and incubated overnight. The junior author smeared, stained, and studied all suspicious colonies at least 18 hours after the start of incubation.

5. All cultures which showed no suspicious colonies after 18 hours were returned to the incubator and checked again 48 hours after the start of incubation before being reported as negative.

Since his graduation from Vanderbilt University School of Medicine in 1943, B. C. Chatham, MD, has been certified by the American Board of Obstetrics and Gynecology. Doctor Chatham is a member of the Central Association of Obstetricians and Gynecologists, a Fellow of the American College of Obstetrics and Gynecology and a Fellow of the American College of Surgeons.

Rex Paty graduated from the University of Oklahoma in 1958. He is a member of the American Society of Medical Technologists and the Oklahoma Society of Medical Technologists.

The following tables show the age distribution of the sixty women studied:

Up to 15	0
16-20	10
21-25	15
26-30	9
31-35	9
36-40	3
41-45	0
46-50	1
over 51	13

RESULTS: One patient, aged 25, had a positive culture for gonorrhea. She was treated with "Vibramycin"® 100 mg. every twelve hours for seven days. Repeat culture then was negative for gonorrhea.

CONCLUSIONS

1. In the private practice of one physician the incidence of unsuspected gonorrhea for two weeks in 60 patients was one case.
2. No teenage patient was found to have gonorrhea.
3. If there is a high incidence of gonorrhea in women in this practice area they did not see the senior author during the study period.
4. Some special campaign will have to be instituted if unsuspected cases of gonorrhea are to be found and treated.

N.B. Dates of this investigation have been omitted in the interest of patient anonymity. □

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Indications: Relief of anxiety and tension; adjunctively in various disease states in which anxiety and tension are manifested; and to promote sleep in anxious, tense patients.

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Warnings: *Drug Dependence:* Physical and psychological dependence and abuse have occurred. Chronic intoxication, from prolonged use and usually greater than recommended doses, leads to ataxia, slurred speech, vertigo. Carefully supervise dose and amounts prescribed, and avoid prolonged use, especially in alcoholics and addiction-prone persons. Sudden withdrawal after prolonged and excessive use may precipitate recurrence of pre-existing symptoms (e.g., anxiety, anorexia, insomnia) or withdrawal reactions (e.g., vomiting, ataxia, tremors, muscle twitching, confusional states, hallucinosis; rarely convulsive seizures, more likely in persons with CNS damage or pre-existent or latent convulsive disorders). Therefore, reduce dosage gradually (1-2 weeks) or substitute a short-acting barbiturate, than gradually withdraw. *Potentially Hazardous Tasks:* Driving a motor vehicle or operating machinery. *Additive Effects:* Possible additive effects between meprobamate, alcohol, and other CNS depressants or psychotropic drugs. *Pregnancy and Lactation:* Safe use not established; weigh potential benefits against potential hazards in pregnancy, nursing mothers, or women of childbearing potential. Animal data at five times the maximum recommended human dose show reduction in litter size due to resorption. Meprobamate appears in umbilical cord blood at or near maternal plasma levels, and in breast milk at levels 2-4 times that of maternal plasma. *Children Under Six:* Drug not recommended.

Precautions: To avoid oversedation, use lowest effective dose, particularly in elderly and/or debilitated patients. Consider possibility of suicide attempts; dispense least amount of drug feasible at any one time. To avoid excess accumulation, use caution in patients with compromised liver or kidney function. Meprobamate may precipitate seizures in epileptics.

Adverse Reactions: *Central Nervous System:* Drowsiness, ataxia, dizziness, slurred speech, headache, vertigo, weakness, paresthesias, impairment of visual accommodation, euphoria, overstimulation, paradoxical excitement, fast EEG activity. *Gastrointestinal:* Nausea, vomiting, diarrhea. *Cardiovascular:* Palpitations, tachycardia, various forms of arrhythmia, transient ECG changes, syncope; also, hypotensive crises (including one fatal case). *Allergic or Idiosyncratic:* Usually after 1-4 doses. Milder reactions: itchy, urticarial, or erythematous maculopapular rash (generalized or confined to groin). Others: leukopenia, acute nonthrombocytopenic purpura, petechiae, ecchymoses, eosinophilia, peripheral edema, adenopathy, fever, fixed drug eruption with cross reaction to carisoprodol, and cross sensitivity between meprobamate/mebutamate and meprobamate/carbromal. More severe, rare hypersensitivity: hyperpyrexia, chills, angioneurotic edema, bronchospasm, oliguria, anuria, anaphylaxis, erythema multiforme, exfoliative dermatitis, stomatitis, proctitis, Stevens-Johnson syndrome; bullous dermatitis (one fatal case after meprobamate plus prednisolone). Stop drug, treat symptomatically (e.g., possible use of epinephrine, antihistamines, and in severe cases corticosteroids). *Hematologic:* Agranulocytosis and aplastic anemia (rarely fatal), but no causal relationship established. Rarely, thrombocytopenic purpura. *Other:* Exacerbation of porphyric symptoms.

Usual Adult Dosage: 1200 to 1600 mg daily, in three or four divided doses; doses above 2400 mg daily not recommended.

Overdosage: Suicidal attempts with meprobamate, alone or with alcohol or other CNS depressants or psychotropic drugs, have produced drowsiness, lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse, and death. Empty stomach, treat symptomatically; cautiously give respiratory assistance, CNS stimulants, pressor agents as needed. Meprobamate is metabolized in the liver and excreted by the kidney. Diuresis and dialysis have been used successfully. Carefully monitor urinary output; avoid overhydration; observe for possible relapse due to incomplete gastric emptying and delayed absorption.

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Observations of Fibrin Split Product Levels in the D.I.C. Syndrome and Other Disease States

LENARD A. POPLIN, MD
JANE SELF, MD

Art or Science! Experiences with newer tests identifying abnormal fibrin split products and their relationship to the clinical syndrome of disseminated intravascular coagulation.

THE PARADOXICAL clinical picture of hemorrhagic diathesis and thrombotic events associated with a prolonged prothrombin time, *i.e.*, decrease in labile clotting factors, decreased fibrinogen, erythrocyte fragmentation, and demonstration of fibrin split products, are the hallmarks of the disseminated intravascular coagulation syndrome (D.I.C.) which is also referred to as consumptive coagulopathy. It is presently felt that this syndrome is best treated with heparin; thus, an accurate diagnosis is of a paramount importance since inappropriate use of this drug could yield catastrophic results.

The tanned red cell hemagglutination inhibition test and the staphylococcal clumping test have been established as the most reliable and sensitive test for detecting fibrin split products, especially fragments I and II.[1] The staphylococcal clumping test has proved to be technically much simpler and therefore more suitable for a community hospital laboratory.[2] Whether the presence of fibrin split products is pathognomonic for the diagnosis of disseminated intravascular coagulation is unclear. The perplexing problem for the clinician is to discover if anything *is* diagnostic of the disseminated intravascular coagulation syndrome and, more specifically, if the presence or absence of elevated fibrin split products is a pivotal point in that decision. The purpose of this report is directed toward answering that question.

The following are brief summaries of four cases illustrating frustrations in correlating clinical and laboratory findings with appropriate therapeutic regimens.

CASE I; D.A:

This patient was a seven-year-old Caucasian girl admitted to Saint Francis Hospital on July 4th, 1971 with a one-week history of fever, myalgia and a petechial skin rash starting on the palms and soles and spreading centrally. The diagnosis of rocky mountain spotted fever was made by the finding of a Proteus OX19 titer changing from negative to positive at 1:160. This was correlated with a history of recent tick bites. The hospital course was complicated by the development of an anemia and azotemia unrelated to blood loss. The admission hematocrit was 38 percent and on the tenth hospital day had fallen to 28 percent. The BUN rose from normal levels to 50 mg.

From Saint Francis Hospital, Tulsa, Oklahoma. Support provided by the W. K. Warren Research Center, Inc.

percent on the sixth hospital day. The peripheral smear showed severe erythrocyte fragmentation. Other studies obtained included a prothrombin time 19.5 sec (control 12 sec), and a partial thromboplastin time 170 sec (normal 30-45 sec). The staphylococcal clumping test for fibrin split products revealed normal values on several determinations.

Comment: We believe this case represents an example of the D.I.C. syndrome associated with rocky mountain spotted fever. The finding of normal amounts of fibrin split products with severe thrombocytopenia, significant prolongation of the prothrombin time and partial thromboplastin time, and severe erythrocyte fragmentation is paradoxical and unexpected. The patient was treated with antibiotics and a short course of heparinization. Recovery was complete.

CASE II; C.B:

This patient was a 65-year-old Caucasian woman who was well until approximately one week prior to admission when she developed a petechial rash on the legs. She was hospitalized in a local hospital but transferred to Saint Francis Hospital following a syncopal episode and sensorium changes. On admission at Saint Francis, her temperature was 101 degrees, B.P. 130/90mmHg, P.-100, and she had a widespread petechial rash. Her sensorium was cloudy, but there were no focal neurological changes. Laboratory studies revealed HgB 9.4 gm%, Hct. 29%, WBC 9,900/cumm; differential count was normal, although the peripheral smear showed numerous red cell fragments. Platelet count ranged around 30,000/cumm; prothrombin time 12.5 sec (control 12.5 sec), PTT 28.5 sec and the fibrin-index was normal. The tanned red cell hemagglutination inhibition test for fibrin split products was positive. The patient demonstrated a bleeding diathesis with marked subcutaneous ecchymosis and some gastrointestinal bleeding. She was treated with heparin and corticosteroids but expired on the third hospital day. Autopsy examination revealed a large retroperitoneal hematoma and focal hemorrhages in the myocardium and lungs, in addition to the gastrointestinal bleeding. Microscopically there were widespread hyaline thrombi in the small vessels.

Comment: This case is believed to represent a case of thrombotic thrombocytopenia purpura with a bleeding diathesis and laboratory evidence of D.I.C. with thrombocytopenia, erythrocyte fragmentation, and positive test for fibrin split products, but normal prothrombin and partial thromboplastin times.

CASE III; L.W:

This patient was a 41-year-old Caucasian man who was apparently in good health until approximately two days prior to admission when he awoke with a "hangover." Ethanol consumption had been excessive the night before. His symptoms consisted of malaise, myalgia, cephalgia, fever and chills. After admission to his local hospital his illness progressed rapidly with a petechial eruption, acrocyanosis and hypotension. His platelet count was 150,000/cumm, prothrombin time 27 sec (control 14 sec), PTT 134 sec (normal 45 sec), fibrinogen 544 mg%, and screening test for fibrin split products negative. Clinically a bleeding diathesis was evidenced by hematemesis, hemorrhagic necrosis of the scrotum and a large hematoma at the site of an arterial puncture. Post mortem examination showed the cause of death to be subarachnoid hemorrhage. Microscopic examination showed numerous hyaline thrombi within vessels of the skin, brain and renal glomeruli.

Comment: This case represents a case of purpura fulminans with disseminated intravascular coagulation syndrome and bleeding diathesis. The laboratory findings in this case are to be contrasted with Case II, thus pointing out the diagnostic and therapeutic dilemmas the clinician finds himself

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in with these inconsistent laboratory parameters.

CASE IV; G.K:

This patient was a 12-year-old Caucasian boy who was admitted to another hospital on March 12th, 1971 with a two-day history of anorexia, abdominal pain, nausea and vomiting. He was a pale, mildly icteric, hypertensive child having a hemoglobin of 8.2 gm% and hematocrit of 22%. The urine revealed 4+ albuminuria and microscopic hematuria; BUN-84 mg%, and a platelet count of 17,000/cumm. Peripheral smear showed erythrocyte fragments, helmet forms and schistocytes. Fibrinogen was normal, but the Fi test[3] was positive. Treatment included peritoneal dialysis, steroids and a course of heparin which was stopped when central nervous hemorrhage occurred. The patient was transferred to Saint Francis Hospital on May 13th, 1971 with a blood pressure of 150/120mmHg. The uremia persisted and responded only to hemodialysis. Hematologic studies at this hospital repeatedly showed a normal prothrombin time, partial thromboplastin time and fibrinogen, but a thrombocytopenia in the range of 40-60,000/cumm. The staphylococcal clumping test for fibrin split products was markedly elevated throughout the hospital stay with successive levels of 61.4mg, 123mg, 245mg, 113mg, and 53mg, (normal 0-7 mg). No hemorrhagic diathesis was present.

Due to persistent renal failure, uncontrollable hypertension, and hemolytic anemia an open renal biopsy was performed. The histologic pattern was that of severe end-stage glomerular disease, thus bilateral nephrectomy was performed. Subsequent renal transplantation has been carried out.

Comment: This case of the hemolytic-uremic syndrome presented many problems. The marked elevation of fibrin split products and evidence for normal labile clotting factors without clinical bleeding, again emphasized the non-specificity of this test in diagnosing the disseminated intravascular coagulation syndrome. It has been pointed out that fibrin degradation products are usually found in the blood of these patients without other evidence of intravascular coagulation.[4, 5] Fibrin degradation products also have been found commonly in patients with primary renal disease,[6, 7] and probably result from lysis of fibrin deposited in the renal vessels. It is of interest that in this patient, fibrin split products have remained elevated after bilateral nephrectomy. The platelet count returned to normal the first post-operative day. The presence of the silastic arterio-venous shunt and periodic hemodialysis may explain this finding.

We have measured fibrin split products using the staphylococcal clumping test pre-operatively and on the first postoperative day in nineteen patients admitted for a variety of elective surgical procedures. Four of the nineteen demonstrated minimal elevations (one or two tube dilutions) pre-operatively. These patients included a 49-year-old woman with idiopathic thrombocytopenic purpura admitted for splenectomy; a 28-year-old woman admitted for bilateral saphenous vein stripping; a 37-year-old man with an inguinal hernia and a 52-year-old man with cholecystitis and pancreatitis.

Seven of the nineteen patients demonstrated elevated levels of fibrin split products on the first postoperative day although two of these had pre-operative elevations. The other five included a 41-year-old woman following inguinal herniorrhaphy; a 42-year-old woman after a radical mastectomy; a 35-year-old woman after a breast biopsy; a 25-year-old man after an inguinal herniorrhaphy and a 56-year-old woman following cholecystectomy. All of the nineteen patients in this series had uncomplicated postoperative recoveries.

We also studied ten critically ill patients in the intensive care unit, for the presence of fibrin split products. Six of the ten had elevated levels. None of these patients had clinical evidence of a bleeding disorder, although two of the patients had markedly elevated levels. A 75-year-old Caucasian woman was admitted with a traumatic subdural hematoma which was surgically evacuated. Fibrin split products measured on the fifth post-operative day were 7,607mg/ml. (normal, 0-7 mg./ml). The other patient was an 82-year-old Caucasian man who was involved in an auto accident, suffering a cervical cord injury with quadraplegia and a ruptured spleen. Fibrin split products meas-

ured four days post-splenectomy equaled 15,214 mg./ml (normal 0-7 mg./ml). The other four patients demonstrated only mild elevations of fibrin split products. None of the six patients had clinical or other laboratory evidence suggesting the presence of disseminated intravascular coagulation syndrome.

It has been pointed out that the hemagglutination inhibition test, although extremely sensitive, does not differentiate between degradation products of fibrin and fibrinogen; therefore, positive results must be evaluated in conjunction with other laboratory data. From the observations reported in this paper it would seem that the presence or absence of elevated fibrin split products does not appear to be pivotal in the diagnosis of the disseminated intravascular coagulation syndrome. Elevated levels may be found in a variety of situations other than D.I.C. Likewise normal values have been found in patients with the unequivocal "syndrome" with bleeding diathesis. The clinician therefore, must rely on the clinical picture as the major indicator in deciding for or against the use of anticoagulation in treating the disseminated intravascular coagulation syndrome. □

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WATCH FOR PROGRAM AND COMPLETE DETAILS IN THE APRIL ISSUE OF

THE JOURNAL

News From The Oklahoma State Department of Health

RABIES PROPHYLAXIS IN SEVERE EXPOSURE

Severe exposure to rabies is defined by two criteria: (1) severity of wound, and (2) location of wound. Severe exposure has been defined by the Public Health Service Advisory Committee on Immunization Practices as "multiple or deep puncture wounds, or any bites on the head, face, neck, hands, or fingers." Severe exposure to rabies may also occur if puncture wounds or lacerations are received in the process of examination or necropsy of a rabid animal, and if the wound is contaminated with saliva or cranial cavity fluids. Bone chips or instruments used in opening animal heads may inflict such wounds. Salivary or cranial cavity fluid contamination of *pre-existing* wounds constitutes *mild* exposure and calls for the appropriate prophylaxis.

Post-exposure prophylaxis of severe rabies exposure should include both passive and active immunization. Passive immunization (antirabies hyperimmune serum) is recommended for most exposures classified as severe, and for *all bites* by rabid animals and *unprovoked bites* by wild carnivores, skunks and bats. When indicated, antirabies serum should be used regardless of the interval between exposure and treatment.

For active immunization in severe exposure, 21 doses of vaccine (duck embryo) are recommended. These may be given as 21 daily doses or 14 doses in the first seven days (either as two separate injections or a double dose). In addition, two booster doses, one ten days and the other at least 20 days after the completion of primary course are recommended. The booster doses are particularly important if antirabies serum was used in the initial therapy.

When rabies vaccine must be given to a person with a history of hypersensitivity, antihistaminic drugs should be given. Epinephrine is helpful in anaphylactoid reactions. If serious allergic manifestations preclude continuation of prophylaxis with one vaccine, the other may be used. If meningeal or neuroparalytic reactions develop, vaccine should be discontinued altogether.

COMMUNICABLE DISEASES IN OKLAHOMA FOR JANUARY, 1972

Disease	Jan. 1972	Jan. 1971	Dec. 1971	Total to Date 1972	Total to Date 1971
Amebiasis	1	4	—	1	4
Brucellosis	—	—	—	—	—
Chickenpox	37	24	62	37	24
Encephalitis, infect.	—	3	3	—	3
Gonorrhea	759	592	763	759	592
Hepatitis, infect. & serum	40	62	161	40	62
Leptospirosis	—	—	2	—	—
Malaria	—	17	1	—	17
Meningococcal infections	—	—	1	—	—
Meningitis, aseptic	1	4	2	1	4
Mumps	31	22	32	31	22
Rabies in animals	8	26	11	8	26
Rheumatic fever	1	3	—	1	3
Rocky Mt. spotted fever	1	1	—	1	1
Rubella	—	13	1	—	13
Rubella, congenital syn.	—	—	—	—	—
Rubeola	1	224	2	1	224
Salmonellosis	3	22	13	3	22
Shigellosis	1	15	18	1	15
Syphilis	80	136	80	80	136
Tetanus	—	—	—	—	—
Tuberculosis, new active	14	22	26	14	22
Tularemia	—	—	3	—	—
Typhoid fever	—	—	—	—	—
Whooping cough	1	3	6	1	3

OSMA JOURNAL/special

The Story of Penicillin

HARRIS D. RILEY, Jr., MD

This article describes the historical details of one of the most important developments in the history of modern medicine—the discovery of penicillin.

ONE OF THE most significant and dramatic advances in medicine came with the introduction and use of antibiotics. Perhaps more than any other group of drugs, antibiotics have changed the pattern of treatment of infectious diseases and have given hope of longer life to countless millions of people. Of the innumerable antimicrobial agents currently available, none have had a greater impact than that of penicillin. Although the introduction of penicillin and of the antibiotic era may have seemed sudden and spectacular to the public, behind it lay many years of effort and experimentation by many men and women in many different countries. However, of all of these the contribution of Alexander Fleming is the most noteworthy.

ALEXANDER FLEMING—EARLY DAYS

Alexander Fleming, always known as 'Alec,' was the youngest one in a family of eight; he was born at Lochfield, an upland farm near Darvel in Ayrshire, Scotland on August 6th, 1881. He had his early schooling in a small country school at Loudon Moor, then at Darvel four miles distant, and after that for 18 months at Kilmarnock Academy. This isolated background likely accounted for his shyness and reserve, and for his great love of nature, which may in turn have directed him into biological science and medicine. Certainly it laid the formulation for his becoming a naturalist. His father died when he was seven years old and at 14 years of age Fleming went to live with a doctor brother in London where he continued his education for two years by attending the Polytechnic Institute in Regent Street. The next four years were spent as a clerk in a shipping office in London. When the Boer war broke out in 1900, he joined the London Scottish regiment as a private, along with two of his brothers. At the age of twenty, on the advice of his brother and with the help of a small legacy from an uncle, 'Alec' Fleming, in 1901, became a student at St. Mary's Hospital Medical School in London. He chose the St. Mary's Hospital Medical School chiefly because of his love for athletics. Unlike American schools, medical schools in Britain, especially in London, emphasized athletic competition. Roger Bannister, a physician and the first person to run the mile in less than four minutes, was a later graduate of St. Mary's. In addition to his athletic prowess, Fleming

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was an excellent student and at St. Mary's compiled a distinguished record. In 1908 he qualified MB, BS of London University with honors in five subjects and the University Gold Medal, and a year later he became a Fellow of the Royal College of Surgeons, having taken the primary examination as a student. He early declared his interest in communicable disease by writing an assay on acute bacterial infections which won him the Cheadle Gold Medal offered by the school. Following graduation, he was persuaded by Doctor John Freeman to apply for a post in the innoculation department at St. Mary's. In 1908 he was accepted as a trainee in bacteriology at St. Mary's and there he was to remain for the remainder of his life.[1, 2, 3]

FLEMING AND WRIGHT

At the turn of the century, Almroth Wright, an Irishman in his early forties who had been educated in Europe, established a small department of research at St. Mary's which was to become one of the first nurseries for the infant science of bacteriology in England. He was to exert a great influence on Fleming's career. Wright was able to create something much greater than a department of research, unusual as that was at the time. He formed a school of thought which fostered the philosophy, originated by Metchnikoff, of direct observation of the mechanism of natural defense against infection and of the practicability of prevention and cure. It was to this school that several thoughtful men were attracted in their formative years, among them Alexander Fleming. Here his mind was prepared for the observation which led to the discovery of penicillin.[2, 3, 4]

For the next few years, Fleming studied and applied Wright's immunologic techniques but, unlike Wright, he accepted chemotherapy rather than immunotherapy as a means of treating infection. He was one of the first in England to use Ehrlich's newly-discovered arsphenamine in the treatment of syphilis. In 1914 he became a medical officer in the Royal Army Medical Corps and served under Wright in a laboratory in Belgium established for the purpose of devising methods to control wound infection. He was particularly impressed by the failure of all antiseptics to sterilize wounds without damaging tissue or killing leukocytes.[3]

After the war, Fleming, now married, returned to the research department at St. Mary's Hospital. In 1922, fourteen years after he had joined Wright, he reported his first significant scientific contribution. This was the discovery of a bacteriolytic substance (christened "lysozyme" by Wright) in mucus, tears and other secretions as well as in egg albumin, plants and skin.[5] With Allison and Ridley, he attempted to extract and purify the active principle but without success. He also showed that lysozyme was present in phagocytes and that staphylococci could acquire resistance to it on exposure. He always maintained his interest in lysozyme and said in later years that it could be more important than penicillin.[3, 5]

THE PENICILLIN STORY

The story of Fleming's chance observation that a contaminant mold of the Penicillium family produced a substance inhibitory to staphylococci is now a classic.

Background: The essential stimulus in Fleming's work was his determined search for an antiseptic that was destructive for bacteria but harmless for the tissues and body fluids. Pure chance deposited this substance on his bench but had he not been prepared because of his training and concepts, he would not have recognized the unknown visitor for what it was. This was in 1928 and it is pertinent to review the status of knowledge of the management of infections and of Fleming's activities at that time.

The antibiotic activity which Fleming had observed and studied was not new in principle. For countless years a home-remedy practice in many lands had been to use moldy bread as a poultice. The Mayans had used a mold from corn for intestinal troubles. The phenomenon known as antibiosis had already been described by many scientists, including Lister,[6], Roberts,[7] Tyndall,[8] Pasteur and Joubert,[9] Babes[24] and several others during the period 1871 to 1885. Gossio[10] in 1925 had worked with Penicillium mold. The therapeutic possibilities of antibiosis—the word

seems first to have been used in France—appealed to French scientists who had always been attracted by medicinal substances of natural origin. Manassein and Polothebnow had treated wounds with molds in 1871, the year Lister had noted his observations. Metchnikoff, like Pasteur, had described the process of antibiosis; and it had been given its name by Vuillemin in 1889. Ten years later, Emmerich and his collaborators had isolated a bactericidal substance, pyocyanase. Florey[24] states that Lodi in 1903 described investigations of an accidental contaminant, a gram-positive coccus, which inhibited *Staph. aureus* and was not toxic to animals. In the early 1900's, Professor M'Fadyean at The Royal Veterinary College commented to his students that strains of staphylococci adjacent to a contaminating fungoid growth on a culture plate had been inhibited.[26] Scott[29] states that in 1912 he observed a similar finding in his laboratory. Twort in 1915 and d'Herelle in 1917 had reported on bacteriophages. In the interim, many other researchers had contributed to the growing literature on the subject.[18]

At the end of the nineteenth century, research was proceeding on these lines but had been unfruitful.[3] The first world war had brought into prominence the fact which had been recognized by Lister that no antiseptic was known that was ideal for dressing wounds. The question, whether antiseptics did more harm than good when applied to septic war wounds, was investigated extensively during World War I by Wright and his collaborators, including Fleming. Following this line of work Fleming investigated the influence on leukocytes and bacteria of many of the antiseptics which were then popular. His observations led him to a clear recognition of the undesirability of using antiseptics which, at best, were as toxic to the tissue cells as to the bacteria. He perceived the importance of the condition that the leukocytes should remain viable in concentrations of the antiseptic which would inhibit or kill bacteria, and demonstrated the unsuitability from this aspect of many of the antiseptics then known.[2]

Discovery: Maurois[2] provides an excellent description, based on the recollection of eyewitnesses, of the events leading up to and during Fleming's epochal observation. Fleming's laboratory at St. Mary's was small and cluttered (Figure 1). An accumulation of culture dishes was piled in apparent disorder, though he could always find the one he wanted without a moment's hesitation. His door was almost always left open and any young research worker in need of assistance was given a warm welcome. Fleming would stretch out an arm, lay his hand at once on the required culture, give it to the intruder, and then usually without uttering a word, go back to his work. When the air in the tiny room became stifling he would open the window which looked on Praed Street.



Figure 1. Fleming's original laboratory at St. Mary's Hospital. Courtesy of Doctor Thomas E. Oppe, Professor of Pediatrics, St. Mary's Hospital Medical School.

In 1928 he agreed to contribute an article on the staphylococci to a vast undertaking—A SYSTEM OF BACTERIOLOGY—to be published by the Medical Research Council. Sometime before this, his colleague, Marlin Pryce had, while working with him devoted a certain amount of study to some abnormal forms, mutants of these microbes.

Fleming, who liked nothing better than to give a helping hand to the young, wanted to quote Pryce in his article. But the latter had left Wright's department before he could complete his researches. Being a conscientious scientist Fleming did not want to publish his results without verifying them, and his new job gave him insufficient leisure in which to do this quickly. Fleming, therefore, had to work over again the ground already covered by Pryce, and set himself to studying numerous colonies of staphylococci. In order to examine these colonies, cultivated on agar in Petri dishes, he had to lift the lids of the dishes and leave the

contents for some considerable time exposed under the microscope, which meant running a risk of contamination.

One day in 1928, Pryce went to see Fleming in his small laboratory where he found him, as usual, surrounded by innumerable laboratory dishes. Fleming disliked being separated from his cultures before he was quite certain that there was no longer anything to be learned from them. He was often teased about his disorderly habits. He was now to prove that disorder may have its uses. With his rough humor he reproached Pryce for obliging him to re-do a long job of work and, while speaking, took up several old cultures and removed the lids. Several of the cultures had been contaminated with mold —a not unusual occurrence. "As soon as you uncover a culture dish something tiresome is sure to happen. Things fall out of the air." Suddenly, he stopped talking. Then, after a moment's observation, said, in his usual unconcerned tones: "That's funny . . ." On the culture at which he was looking there was a growth of mold, as on several of the others, but on this particular one, all around the mold, the colonies of staphylococci had been dissolved and, instead of forming opaque yellow masses, looked like drops of dew. (Figure 2)

Pryce had often seen old microbial colonies which for various reasons had dissolved. He thought that probably the mold was producing acids which were harmful to the staphylococci — no unusual occurrence. But, noticing the keen interest with which Fleming was examining the phenomenon, he said: "That's how you discovered lysozyme." Fleming made no answer. He was busy transferring a piece of the mold with his scalpel and putting it in a tube of broth. Then he picked off a scrap measuring about one square millimeter which floated on the surface of the broth. He obviously wanted to make quite sure that this mysterious mold would be preserved.

"What struck me," Pryce says, "was that he didn't confine himself to observing, but took action at once. Many people observe a phenomenon, feeling that it may be important, but they don't get beyond being surprised—after which, they forget. That was never the case with Fleming." Pryce remembers another incident, also from the time he was working with him.[2] "One of my cultures had not been successful, and he told me to be sure of getting everything possible out of my mistakes. That was characteristic of his whole attitude to life."

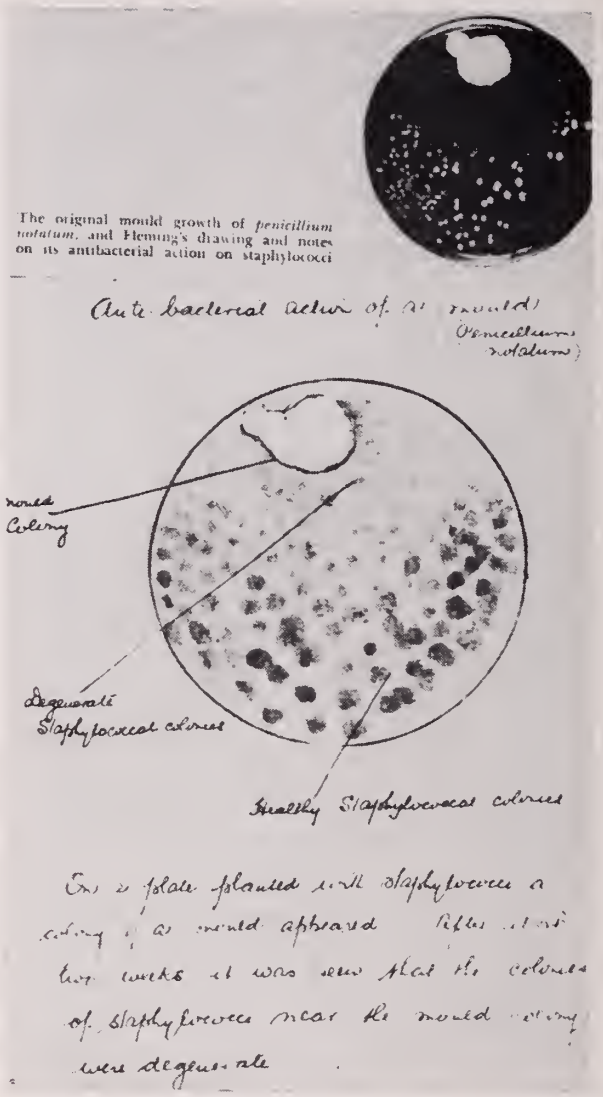


Figure 2. The original mold growth of *Penicillium notatum*, and Fleming's drawings and notes on its antibacterial action on staphylococci. From Maurois.[2]

Fleming put the Petri dish aside. He was to keep it as a precious treasure for the rest of his life. He showed it to one of his colleagues. "Take a look at that," he said, "it's interesting—the kind of thing I like; it may well turn out to be important." The colleague in question looked at the dish, then handed it back with a polite: "yes, very interesting." But Fleming, in no way discouraged by this manifestation of indiffer-

ence, temporarily abandoned his investigation of the staphylococci, and gave himself entirely to studying the surprising mold.[2]

Fleming later described his discovery as follows:[26]

> When I first noticed the action of penicillin, I was playing with a culture of staphylococcus, doing nothing very important. Actually, what had happened was that I had contracted to write the chapter of a book on staphylococcus. A man had written saying that by certain methods he could make the colonies of staphylococcus appear not a bit like themselves. I was trying to see whether he was telling the truth. I had some culture plates of staphylococcus, looked at them occasionally under a microscope, put the cover back on and set them aside for a while. When some people have finished with a culture plate they throw it aside, and that is the end of it. They miss a lot of peculiar things that happen by accident. I didn't throw those plates away, and later on they became contaminated. Of course, if you take off the cover of a culture plate things get in from the air. One of these plates got contaminated with a mold. That wasn't unusual. We had often had plates contaminated with molds before and hadn't paid much attention to them, except to use appropriate language and throw them away. But this time there was something different on the plate. The mold itself wasn't a bit unusual. The microbes in the neighborhood of that mold colony seemed to be dissolving. That was worth paying attention to. At least I thought it was, and I didn't pursue the original staphylococcal research. I touched that mold with a platinum wire and transferred some of the spores to another tube, off by themselves; there we had a pure culture of the mold that we could keep and experiment with. I knew nothing at all about molds at that stage of the proceedings. A mold starts off with a little spore, a tiny thing, smaller than a red blood corpuscle. When it grows it sends out a sprout or two, which branch again and again to produce the mass of mold that you recognize on bread, or cheese, for example.
>
> We then tried to see what this mold did. One of the first steps, an easy one, was to put it on another culture plate. You take a fresh culture plate, plant the mold and let it grow in the room. You don't want an incubator for this; an ordinary room will do beautifully for mold. Just let it grow for three or four days. Next we took different microbes, whichever were handy, and streaked them across the plate up to the mold. Some of them grew right up to the mold; some of them didn't go anywhere near it. So here we had a mold that made something which diffused out into the agar and stopped the growth of some of the microbes, but not of others.

An occurrence such as that which Fleming witnessed had been observed previously;[24, 26] the importance lay less in Fleming's observation than in his action. According to Stewart,[3] Fleming felt in an entirely unpretentious way that destiny entered his laboratory that day; not least among his endearing qualities was his candid admission, years later, that 'the fates were wonderfully kind to me.' Maurois[2] stated:

> His frame of mind at the time and his subsequent activities are less well recognized, though no less important than the chance observation. It is clear that the importance of the observation was soon registered in Fleming's well-prepared mind; not only did he take the essential steps of testing and preserving the mold, he also gave up many other activities so that he could concentrate his attention on the phenomenon which he had encountered. It is fortunate for mankind that he had the intelligence and the opportunity to do so, though he had been criticized—for not mustering more energy in his research.

Fleming, himself, stated: "It was fortunate that . . . I was always on the lookout for new bacterial inhibitors, and when I noticed on a culture plate that the staphylococcal colonies in the neighborhood of the mold had faded away, I was sufficiently interested in the antibacterial substance produced by the mold to pursue the subject."[27]

On the other hand, Florey[24] states that nothing emerges from Colebrook's memoir[28] or from Fleming's own writing to suggest that he had in mind the idea that penicillin might be a systemic chemotherapeutic agent. Fleming has stated: "I had no suspicion that I got a clue to the most powerful therapeutic substance yet used to defeat bacterial infections in the human body. But the appearance of that culture plate was such that I thought it should not be neglected."[27]

There can be little doubt that Fleming, along with his chief, Almroth Wright, was obsessed with and clung tenaciously to the hypothesis that the effective antiseptic for wounds must be destructive for microorganism without harming the tissues of the host. Certainly his adherence to this concept with lysozyme allowed him to appreciate the possibilities of the activity of his mold. Chance had favored the prepared mind.[21]

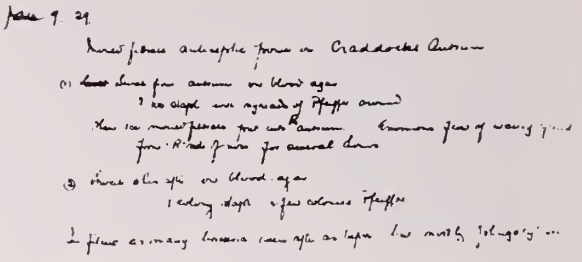
Fleming, proceeding to cultivate the undefined mold, made an extract and studied the activity of the crude "mold broth filtrate" in detail against a variety of pathogenic bacteria and tested its toxicity in animals.[2, 3] Fleming showed that it inhibited the growth of a number of pathogenic microorganisms, i.e., staphylococcus, *Streptococcus pyogenes* and *viridans*, pneumococcus, *C.*

diphtheriae, and the gonococcus and meningococcus. It had a weaker effect on *B. anthracis* and one of the gram-negative bacilli such as *Esch. coli, S. typhi, Ps. aeruginosa*, and *V. chloarae*. Thus, the active agent inhibited the growth of many gram-positive and certain gram-negative cocci. Heating to 80° C or boiling for a few minutes hardly affected the activity of the filtrate, but boiling for one hour reduced its strength to less than one-quarter; this loss was greater if the fluid was alkaline than if it was neutral or very slightly acid. It was found that if the broth were evaporated at a low temperature to a sticky mass the active principle could be completely extracted by absolute alcohol, though not by ether or chloroform. No experiments with such an extract were reported, however.[11]

The rate of production of the inhibitory substance by the fungus and the influence of the composition of the medium on the antibacterial titer of the culture fluid, were studied. From the experiments dealing with the rate of killing of bacteria Fleming considered that the substance belonged to the group of "slow-acting antiseptics."[11]

In other experiments, Fleming demonstrated that the penicillin-containing broth filtrate differed in one important respect from other known antiseptics in that it was more toxic to bacteria than to leukocytes and other animal cells. The work carried out at that time on the crude broth, which contained little active material, was insufficient to show that penicillin was so lacking in toxicity and retained its activity so well in the body that amounts sufficient to inhibit bacteria in the blood stream could be injected. Only after a long series of experiments several years later was its extraordinary combination of desirable properties, which made it an almost ideal chemotherapeutic agent, revealed.

Fleming proceeded to test other fungi, including eight strains of Penicillium, for antibiotic production. The only species which produced a bactericidal substance was a strain of Penicillium identical in appearance and properties to the original mold which was identified at the time as *P. rubrum*, though in subsequent studies it was reclassified by Thorn as *P. notatum*.[3]



'January 9th, 1929: mould filtrate antiseptic power on Craddock's antrum. Swab from antrum on blood-agar: 100 staphylococci with myriads of Pfeiffer around. Then 1 c.c. mould filtrate put into right antrum. Swab three hours after on blood-agar. One colony of staphylococci and a few colonies of Pfeiffer. In films as many bacteria seen after as before but mostly phagocytosed.'

Figure 3. Fleming's original laboratory notes on the first use of penicillin. Modified from Maurois.[2]

Despite these experiments, the mold extract had not as yet been used in humans. In January, 1929, Stuart Craddock, a laboratory assistant who had been working with Fleming in his efforts to find a suitable antiseptic, developed acute sinusitis. Figure 3 depicts a quotation from Fleming's notebook describing his first attempt to treat human infections with penicillin.

Presentation to the Scientific Community: Meanwhile, Fleming had prepared a paper on penicillin which he read on February 13th, 1929, to the Medical Research Club. Sir Henry Dale, who was then its chairman, remembers the reactions of the audience. They were more or less the same as they had been in the case of lysozyme. "Oh, yes, we said, Fleming does observe that sort of nice thing." It is certainly true that he never knew how to present findings in the best light. "He was very shy, and excessively modest, in his presentation, he gave it in a half-hearted sort of way, shrugging his shoulders as though he were deprecating the importance of what he said. . . . All the same the elegance and beauty of his observations made a great impression." That impression may have been real enough, but nothing in the strangely superior and sullen attitude of his listeners gave any indication of it.[2]

When a paper has been found interesting it is always followed by questions, and the

greater the interest aroused, the more numerous are the questions. The reader stands at his desk, waiting for them. If none comes, that period of waiting in the silent room is a terrible ordeal. Fleming experienced it when he spoke of penicillin, as he had done, formerly, when he spoke of lysozyme. Not a single question was asked, whereas, the next paper, "On the Nature of the Lesion in Generalized Vaccinia," provoked a lengthy discussion. The icy reaction to something which he knew to be of capital importance appalled him. In 1952, when he was at the summit of his fame, he was still talking about "that frightful moment."[2] But in 1929 he gave no sign of disappointment. According to Maurois,[2] "He knew the value of what he had done and that knowledge gave him strength and made it possible for him to remain unshaken in his belief."

Fleming proceeded to prepare for publication the details of his experiments. His original paper on penicillin was published in the *British Journal of Experimental Pathology*[12] in June, 1929 when Fleming was 48 years of age. (Figure 4) Maurois[2] states,

> The paper is a triumph of clarity, sobriety and precision. In a few pages it covers all the facts. It does justice to the efforts made by Ridley to purify the substance. It shows that penicillin, since it can be dissolved in pure alcohol, is neither an enzyme nor a protein. It speaks of the innocuousness of the substance when injected into the blood stream and says that it is more effective than any other antiseptic and can be used in the treatment of infected surfaces. It states that he is engaged in studying its value in the treatment of pyogenic infections.

In this paper, he described in detail the rate and extent of bactericidal activity and noted that the action of penicillin was directed essentially against gram-negative pyogenic cocci, there being little or no action on gram-negative bacilli. (Figure 5) For this reason, he was impressed by the immediate practicability of incorporating penicillin to make blood agar selective for the isolation of Hemophilus in sputum. This was featured in the title of his paper "On the Antibacterial Action of Cultures of Penicillium, with Special Reference to their Use in the Isolation of *B. influenzae*." This title might have been chosen better, for it gave rise to the impression, then and later, that Fleming was not aware of the therapeutic potential of his discovery. As Stewart[3] had pointed out, the text of the paper belies this, for he mentions the lack of toxicity of the antibacterial substance, which he named "penicillin," in the rabbit, mouse, human eye, human leukocytes and wound surfaces. It is also clear in the paper and in notes made soon after, that he tested the therapeutic properties of the crude brew of penicillin in wounds infected with staphylococci. In the summary of the paper, there is a recapitulation of all these points and, in particular, the following: "1. A certain type of penicillin produces, in culture, a powerful antibacterial substance . . . 7. Penicillin is non-toxic to animals, even in massive doses, and is non-irritant. . . 8. It is suggested that it may be an efficient antiseptic for application to, or injection into, areas affected with penicillin-sensitive microbes."

Although his paper in 1929 attracted little attention, Fleming continued to work with his extract and used it extensively as a topical antiseptic. The clinical results were not impressive because of the low potency and instability of the crude material. Attempts by his colleagues, Craddock and Ridley, to purify it by evaporation were unsuccessful. He also failed to arouse any interests in the extract among bacteriologists, physicians or the pharmaceutical industry.

Fleming realized the need to purify the extract so that it could be produced in quantity. He then approached several chemists, including Harold King, Head of the Department of Chemistry at the Medical Research Council's Laboratories at Hampstead. Harold Raistrick, Professor of Biochemistry at the London School of Hygiene and Tropical Medicine, studied penicillin with the help of a bacteriologist, R. Lovell, and another chemist, P. W. Clutterbuck. They succeeded in isolating the inert pigment from the mold, but not the antibacterial substance. Their work came to a halt with Clutterbuck's untimely death.[3]

Meanwhile, Fleming had published another paper dealing with the use of penicillin as a selective agent in media for the isolation of Hemophilus.[14] In 1932, when it was apparent that attempts at chemical extraction and purification were unsuccessful, he published an account of his use of the crude brew as a topical agent in the treatment of infected wounds.[15] In 1932 C. G.

Payne, in Sheffield, obtained a culture of Penicillium from Fleming and used it topically with success in several infections, but his observations were never published.[11] In 1936, Fleming presented a paper and demonstration about penicillin to the Second International Congress of Microbiology.[16] He continued to speak to other scientists about the importance of purifying it by chemical means, but again failed to arouse any obvious interest.[3] How completely the possible use of penicillin in the treatment of septic infection was forgotten is shown by the fact that in reviews on the subject of chemotherapy and antiseptics at the time of the beginning of World War II, penicillin was not mentioned.[11]

After the demonstration in 1935 that antimicrobial activity of prontosil was due to the sulfonamide fraction, Fleming devoted his attention to the study of these new chemotherapeutic agents.[2, 3, 13] It is of interest to inquire why Fleming's work on his discovery ceased, despite his appreciation of the fact that penicillin broth differed so greatly from other antiseptics. In 1940 he said: "We have been using it in the laboratory for over ten years as a method of differential culture. It was used in a few cases as a local antiseptic but although it gave reasonably good results the trouble of making it seemed not worthwhile."[17] Although it seems clear that he was discouraged about the future of penicillin and that his research efforts were diverted in part along other channels, there is no factual foundation that Fleming abandoned penicillin after 1929.[18]

As Stewart[3] has stated, to anyone interested in the evolution of medical science, the events in the years immediately following 1929 are most revealing. In two decades following 1910, no single drug having significant activity against the most widespread class of disease-producing microorganisms —the bacteria—had been developed. Disappointedly, medical men and laymen had begun to regard chemotherapy as an impractical dream. Many physicians saw no possibility—or refused to see any possibility— of treating any major bacterial infection by a drug, though the practicability of systemic chemotherapy had already been demonstrated in syphilis and, with empirical remedies, in malaria and amebic dysentery. And yet, in every general hospital, and especially in children's wards, bacterial infection was by far the greatest challenge to the therapeutic impotence of the day.

> Since the days of Lister, antiseptics had come and gone. None was fit to swallow or inject, though Browning, following Ehrlich's approach had found the flavine acridines to be less toxic than most antiseptics. Hindsight is an easy road to wisdom, but it is nevertheless astonishing to reflect that no one at the time, except Raistrick and an American bacteriologist, R. D. Reid of Baltimore, exhibited active interest in any of Fleming's reports, though to any bacteriologist in those days an impure but nontoxic filtrate killing staphylococa at a dilution of 1:600 must have offered the prospect of a strange new experience. Academic research in medicine is often too fundamental to be concerned with the prevention and cure of disease but, even in sympathetic circles, Fleming's work aroused no interest, nor was there any evidence of exploratory action on the part of the pharmaceutical industry. There are fashions in medical science no less than in costumes; Fleming's observations, reported at a time when therapeutic nihilism was the vogue, were completely ignored. Even Wright, to whom research on infection was a religion, was oblivious to the therapeutic potential of Fleming's work, though perhaps appreciative of its technical accuracy.[3]

Production of Penicillin—The Florey and Chain Team: Meantime, too, destiny was shaping another phase of the approach to antibiotics. Howard Florey, born in Adelaide, Australia, in 1898, studied medicine in his native land and came to Oxford on a Rhodes scholarship. In 1925, the Rockefeller Foundation sent him to the United States to gain experience in a number of laboratories. Upon return to England, Florey heard about the work Fleming had been doing on lysozyme and took an interest in it. In 1935, Florey was appointed to the Chair of Pathology at the Sir William Dunn School in Oxford. This position afforded him excellent opportunities to direct and coordinate research teams, as the school housed laboratories for pathology and bacteriology under one roof—and Florey was competent in each of these.[18]

Shortly after taking over his professorial duties, Florey invited E. B. Chain to organize a biochemical department. Chain was born in Berlin in 1906, of a Russian father and a German mother. At the Friedrich-Wilhelm University in Berlin, Chain special-

ized in biochemistry and physiology, receiving his degree shortly before the Nazis came into power. Of Jewish faith, Chain emigrated to England in 1933, working at the Cambridge School of Biochemistry until he joined Florey in 1935.[18]

Work on the mode of action of lysozyme at the Sir William Dunn School of Pathology led Chain to systematically investigate older literature having to do with bacteriolytic agents.[11] In the course of numerous discussions of lysozyme, Florey and Chain decided to undertake jointly a systematic investigation of some of the antibacterial substances produced by microorganisms.[11, 18] Chain was intrigued by lysozyme and while searching through the literature on antibacterial substances, came upon Fleming's paper on penicillin.

"The first investigations decided upon at Oxford included a study of penicillin, because its relative instability indicated that it might have interesting chemical properties, and because it was stated to be active against the staphylococcus, against which no other effective remedy was known at the time," the research team at Oxford reported in *Antibiotics*.[11] Chain and Falk had begun work on a culture of Fleming's strain of *Penicillium notatum* in 1938; however, it was not until late in 1939 that work on penicillin was taken up vigorously by Florey, Chain, and Heatley.[11, 18]

Gradually, a small store of the impure penicillin was gathered—enough for trials in mice. The first test was made May 25th, 1940. Mice were infected with virulent strains of hemolytic streptococcus. Two groups were injected with penicillin; one group of controls was unprotected. All the control mice were dead after sixteen hours; the penicillin-protected mice survived. Other tests on mice, conducted a few days later, confirmed these results.[18]

Imperfect as they were, the mouse tests stimulated hope for penicillin. Heatley devoted his attention to production of penicillin. A. D. Gardner and J. Orr-Ewing took up bacteriologic investigations; Florey and M. A. Jennings undertook pharmacologic and biologic investigations. Chain, with A. G. Sanders and E. P. Abraham, collaborated on chemical and biochemical aspects. When the stage of clinical trial was reached, H. W. Florey, his wife, Doctor H. E. Florey, and C. M. Fletcher, were responsible. This group formed the nucleus of what came to be called the "Oxford team." Later, several other scientists joined the effort.[11, 18]

Another complication now entered the penicillin picture: World War II. This added to the difficulty of obtaining supplies and apparatus. However, the need for improved medicines to care for the war wounded stimulated researchers to greater efforts—even though bombs were falling on Britain almost nightly.

"Penicillin as a Chemotherapeutic Agent" was the title of the first paper to come from the Sir William Dunn School of Pathology.[19] Published in *The Lancet*, August 24th, 1940, it caught the eye of Fleming. He had never stopped hoping that some day penicillin would be concentrated and purified—and the article was a happy surprise. He had not known of the work going on at Oxford. He was determined to see for himself. Fleming went to Oxford, on September 2, 1940, and called on Florey and Chain in their laboratory. To Chain, it was indeed a surprise—he had thought Fleming was dead! Chain thereafter obtained some of the brown powder for microbiological and clinical purposes at St. Mary's Hospital. Fleming was in touch with the Oxford group from time to time thereafter, but it was the work of the team at Oxford that developed penicillin production to practicality.[18]

Efforts to produce penicillin in larger quantities presented many problems. The mold would grow only on shallow layers of fluid. Wartime demands made it difficult to secure needed apparatus. At first, old-time circular bedpans were pressed into service; later, flat ceramic bottles were used. Extraction apparatus was ingeniously constructed out of available odds and ends, not the least useful of which were milk churns.[18] A counter-current solvent extraction method was devised which yielded, early in 1941, enough penicillin for a preliminary study in humans. The cup-plate assay technique developed by Heatley led to the definition of the Oxford unit of activity (0.6 μg of pure penicillin G), still in use today.[3]

Clinical Trials: The first clinical trial with the crude penicillin powder was conducted on February 12, 1941. The patient

ON THE ANTIBACTERIAL ACTION OF CULTURES OF A PENICILLIUM, WITH SPECIAL REFERENCE TO THEIR USE IN THE ISOLATION OF *B. INFLUENZÆ*.

ALEXANDER FLEMING, F.R.C.S.

From the Laboratories of the Inoculation Department, St Mary's Hospital, London.

Received for publication May 10th, 1929.

WHILE working with staphylococcus variants a number of culture-plates were set aside on the laboratory bench and examined from time to time. In the examinations these plates were necessarily exposed to the air and they became contaminated with various micro-organisms. It was noticed that around a large colony of a contaminating mould the staphylococcus colonies became transparent and were obviously undergoing lysis (see Fig. 1).

Subcultures of this mould were made and experiments conducted with a view to ascertaining something of the properties of the bacteriolytic substance which had evidently been formed in the mould culture and which had diffused into the surrounding medium. It was found that broth in which the mould had been grown at room temperature for one or two weeks had acquired marked inhibitory, bactericidal and bacteriolytic properties to many of the more common pathogenic bacteria.

Figure 4. Reproduction of first page of original article on penicillin by Fleming which appeared in Brit. J. Exp. Path., **10:** 226-36, 1929.[12]

was an Oxford policeman, dying of staphylococcal osteomyelitis and septicemia in the Radcliffe Infirmary, Oxford. Penicillin arrested the infection almost immediately and the patient showed signs of recovery but five days later when all the penicillin had been used, the infection resumed its advance and killed the patient. There are times in human affairs when tragedy clears the path and this fatality, providing two trials in a sense for the price of one, emphasized the need and the urgency for further research upon production.[3]

Enough penicillin was produced at Oxford during the next few weeks for the treatment of five other patients, four of them children with staphylococcal or streptococcal infections who had not responded to sulfonamides or surgical measures. The results were convincing, each in a different way, and the absence of toxicity was almost as impressive as the rapid therapeutic effect.[20] As Stewart[3] states, in the present day when a clinical trial is becoming an exercise in statistics and bureaucracy, there is irony in reflection that the massive efforts which followed were based upon a few toxicity tests in rodents and upon a clinical trial in six selected subjects, two of whom died. Had the toxicity test been extended to guinea pigs, penicillin might have been rejected. Had current regulations been enforced, it would have been ineligible for submission.

The publication in *The Lancet* of the two reports about penicillin excited more interest in Fleming's paper in 1929, but not much more. At Oxford, Professor Trueta was credited with the remark that, when he saw Florey looking at patients, he knew something unusual was happening; in the burn units at Oxford and Glasgow, penicillin was applied topically in minute quantities to eradicate pyogenic cocci—only to open the road to *Pseudomonas pyocyanea*.[3]

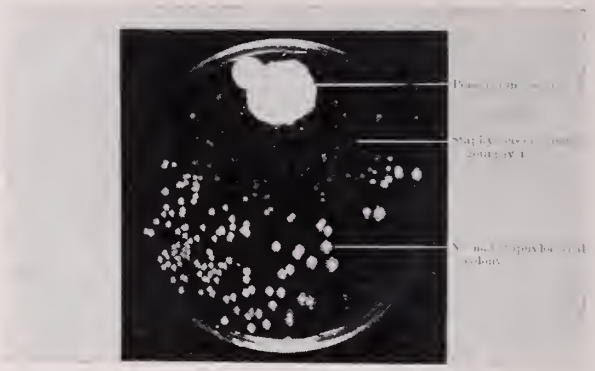


Figure 5. Photograph of culture plate from original article.[12]

Large Scale Production: Pleased as he undoubtedly was at the purification of the active principle. Fleming shared the view of many when he stated that penicillin would be almost useless as a therapeutic agent until synthesized. This was the view held also by those in industry who had been approached in 1940. Laboratory production facilities for penicillin were inadequate, even for clinical testing; and, because of wartime pressures, English pharmaceutical firms felt it impossible to invest the time and equipment needed to perfect mass production. The penicillin content of the crude brew was at most two units/ml; 50 to 80 percent of this was lost in extraction; hence 2,000 liters of fermentation liquor would be required for the treatment of one patient.

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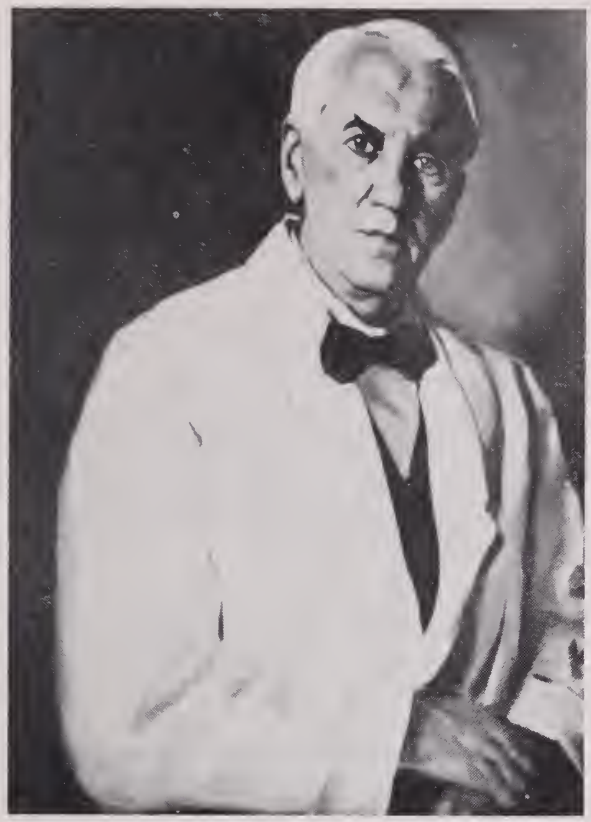


Figure 6. Portrait of Sir Alexander Fleming located at the Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma.

The future seemed to lie with synthesis, but under the conditions prevailing in Britain during the grim phase of war in 1940-41, this could not be contemplated, nor could fermentation vats be made available. After consultation with Weaver of the Rockefeller Foundation it was decided that Florey and Heatley should visit America, which was not yet at war, to see if large-scale production could be contemplated there. With financial support from the Rockefeller Foundation, Florey and Heatley arrived in the United States on July 2, 1941.[3] They were guests of John F. Fulton, Professor of History of Medicine at Yale University. Fulton put them in touch with Ross Harrison, chairman of the National Research Council, who advised them to talk to Charles Thom, of the Bureau of Plant Industry (who years before had identified Fleming's mold as *Penicillium notatum*). Doctor Thom took them to Percy A. Wells of the Department of Agriculture. After learning of the problem, Wells sent Florey and Heatley to the Northern Regional Research Laboratory of the Department of Agriculture at Peoria, Illinois. The problem of producing more penicillin was put to the director of the laboratory, Orville E. May, and to the director of the fermentation division, Robert D. Coghill, on July 14th. Coghill suggested that perhaps the deep-tank fermentation methods then used to produce gluconic acid might be applied to penicillin production.[18]

Heatley remained at Peoria for several months, cooperating in development of production improvements. Florey visited a number of drug firms in the United States and Canada, attempting to interest them in penicillin production, and consulted with governmental agencies. His old friend, A. N. Richards, had become chairman of the Committee on Medical Research of the United States office of Scientific Research and Development. Richards helped materially in stimulating research activity. A number of United States pharmaceutical firms began production of penicillin, among whom were Merck & Company, E. R. Squibb and Sons, Charles Pfizer and Company, Bristol Laboratories, Abbott Laboratories, Winthrop Chemical Company, Cutter Laboratories, and Parke, Davis and Company.[18]

Several advances came from the laboratories in Peoria. First, corn steep liquor was added to the culture medium—and the output of penicillin was stepped up twenty times. Substitution of lactose for glucose further improved the output. A search for better molds was undertaken, and from a rotting cantaloupe found in a Peoria market there was cultured out a species of *Penicillin chrysogenum* that improved yields of penicillin still further. Artificial mutations made the progeny of this strain even more fruitful.[3, 11, 18]

In addition to the work at Peoria, United States pharmaceutical manufacturers began intensive application of mycologic experience gained in other fields—brewing manufacture of citric acid, and other chemicals—to the penicillin problem. Entry of the United States into the war, December 7th, 1941, added further stimulation to the effort. Techniques were developed to produce enormous quantities of the drug by deep-tank fermentation. The government took control of distribution of the entire penicillin output, assuring its availability for war

needs, and for the most urgent civilian needs. Of the tremendous growth of penicillin production, it has been said that, actually, in 1941, there was not sufficient penicillin in the United States to treat a single case; in 1942 there were probably insufficient quantities to treat 100 cases; but, by September, 1943, there was enough to satisfy the demands of the Armed Forces of this country and those of our allies as well.[18] The first report in the United States literature on penicillin appeared in 1941.[22]

There was constant interchange of information between government scientists of both nations. As mass production methods developed, English firms, including Boots Pure Drug Company, British Drug Houses, Glaxco Laboratories, May and Baker, and Burroughs and Wellcome began large-scale production.

Research further revealed that there were several types of penicillin produced by the molds. Chemical methods of refinement replaced the impure brown amorphous powders with pure, crystalline salts. Penicillin F became most popular in England, while penicillin G became standard in the United States. The isolation and production of the nucleus of penicillin has made possible a major breakthrough in medicine—the development of a vast number of semi-synthetic penicillins many of which have characteristics which overcome some of the therapeutic inadequacies of penicillin G.[23]

The Final Years: When Fleming announced his work on lysozyme in 1921, his listeners were barely polite. When he announced his findings on penicillin, in 1929, there was no show of enthusiasm. Nor was there any for another ten years. After Florey and Chain announced their work and penicillin began to become generally available, honors showered upon all of them. Florey was elected a Fellow in the Royal Society in 1941; Fleming was elected in 1943. By 1943 honor after honor was heaped upon Fleming and the "Fleming Myth" had started.[21] Both Fleming and Florey were made Knights Bachelor by the King of England in 1944. Chain also was elected to the Royal Society. In December, 1945, Fleming, Chain, and Florey were jointly awarded the Nobel Prize for Medicine. Honorary degrees were awarded all three.

Fleming became professor of Bacteriology at St. Mary's; was named, first Rector, then Chancellor, of Edinburgh University; and, upon Sir Almroth Wright's retirement, Principal of the Wright-Fleming Institute at St. Mary's, which had been renamed in his honor.

One of Fleming's last visits to the United States was in July, 1949 when he dedicated the Oklahoma Medical Research Foundation at the University of Oklahoma Medical Center in Oklahoma City. The portrait of Fleming which hangs in the lobby of the Oklahoma Medical Research Foundation is depicted in Figure 6.

Florey retired as Professor and Director of the Sir William Dunn School of Pathology in 1962, and became Provost of The Queen's College, at Oxford. He died February 21st, 1968 in Oxford.[25] Chain in 1949 became Head of the International Research Center for General Biochemistry and Chemical Microbiology at the Institute of Public Health of the Italian State, in Rome; and in 1961 was appointed Professor of Biochemistry at the Imperial College of Science and Technology, in London.

But one further event of major interest did occur in the life of Fleming. His wife of 34 years, Sareen, died in 1949. This left Sir Alexander a very lonely man. In 1946, an intelligent Greek woman scientist, Doctor Amalia Coutsouris-Voureka, joined the Institute at St. Mary's. She was devoted to Sir Alexander, and in the spring of 1953, they were married. The concluding chapter of this biography by Maurois is headed, "Too Short a Happiness." On the morning of March 11th, 1955, at the age of seventy-four years, Sir Alexander Fleming quietly died as the result of a myocardial infarction. England honored him once again with burial in the crypt of St. Paul's Cathedral, close to the towering tombs of Wellington and Nelson. □

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Annual Meeting To Stress Science, Economics and the Future

Future changes in the economic, sociologic, and scientific practice of medicine will be the main topics for consideration during the OSMA's 66th Annual Meeting. To be held in Oklahoma City's Skirvin Hotel, the meeting is scheduled for May 18th-20th.

In addition to the usual social events and the featured programs on each day, a number of medical specialties have announced intentions of holding scientific meetings during the three days. These include the anesthesiologists, dermatologists, internists, otolaryngologists, pathologists, pediatricians, and psychiatrists. The Oklahoma Society of Plastic Surgeons, Inc., intends to hold a business meeting for its members.

The five major components of the annual program will be scattered over the three days. The first will be held Thursday afternoon, May 18th, and will be a "Third Party Payment Seminar." This will be a nuts and bolts workshop for physicians or *the person in their office responsible for billing third party carriers.* Representatives from Aetna-Medicare, the Oklahoma Department of Institutions, Social and Rehabilitative Services (DPW), and Oklahoma Blue Shield will be on hand to explain the operation of their program and to answer questions on such topics as proper filing of claims, changing of physicians' fee profiles, contesting a payment decision, justification of higher than usual fees, etc.

The second major portion of the program will take place Friday morning, May 19th. A special "Symposium on Peer Review" will be held at that time to discuss the philosophy of peer review from both the pro and con aspects. Three experts who are already working on peer review programs from other parts of the United States will be present.

Friday afternoon's program will be "Coronary Disease '72" and will feature a trio of speakers from the Mayo Clinic: Robert Brandenburg, MD, Daniel C. Connolly, MD, and Ralph Smith, MD.

The subject of Saturday morning's program on May 20th will be "Health Maintenance Organizations." Popularly known as the HMO, this is a new concept in the delivery of health care that is being promoted by the Nixon administration, the hierarchy of HEW, and by a number of United States Senators and Representatives. The discussion will revolve around what is an HMO, how does it work, how is it financed, and is it really "the answer" to health care delivery.

"The Future of Medicine" will be the subject of the symposium on Saturday afternoon. Four nationally prominent men will bring the program. They include Max Parrott, MD, the knowledgeable and articulate chairman of the AMA Board of Trustees; Richard Wilbur, MD, former Deputy Executive Vice-President of the AMA and now on loan to the United States Department of Defense as an undersecretary; one of the foremost social planners of the day, Wilbur J. Cohen, PhD, who also was a principle architect of Medicare; and Jenkin Lloyd Jones, Editor and Publisher of the Tulsa Tribune, a nationally known syndicated columnist and former president of the U. S. Chamber of Commerce.

In announcing this program Doctor John Blaschke, Chairman of the annual meeting, said "None of these men are timid. They are all nationally recognized for their knowledge, foresight and especially for their forthrightness. We can expect nothing less than an extremely enlightening and lively discussion on Saturday afternoon."

The business aspect of the annual meeting will be limited to Thursday, May 18th, only. In past years the House of Delegates has met on two separate days, but this will be changed this year.

Opening session of the House of Delegates will be held at 8:30 a.m. on Thursday morning. The house will adjourn at 10:00 a.m. for reference committee meetings and then will reconvene that evening at 7:30 p.m. for the closing session. A special reception and dinner for the delegates will be held Thursday afternoon from 5:00 until 7:00 p.m. Speaker for the dinner will be Max Parrott, MD, Chairman of the AMA Board of Trustees.

The reference committee meetings Thursday morning are open to all members of the association and provides an opportunity for them to express their views on its various business aspects.

Social events during the annual meeting will start with hors d'oeuvres and cocktails *al fresco* on Friday evening from 6:00 until 7:30 p.m. around the Skirvin Hotel's Swimming pool. The cocktail reception is planned for everyone attending the meeting and will serve as a gathering place for physicians planning a night on the town or intending to go to one of the special society dinners.

Saturday's picnic luncheon will be sponsored by the Insurance Company of North America. The picnic style spread will include corned beef and ham sandwiches, beer, soft drinks, assorted relishes and side dishes. During the past several years the picnic luncheons have proved to be one of the most popular highlights of the annual meeting.

As always, the 66th annual gathering of Oklahoma's doctors will be capped off Saturday evening with a reception and the President's Annual Dinner-Dance. Cocktails and conversation will be the bill of fare

during the reception to be followed by a dinner-dance in the hotel's Persian Room. It is traditional that the banquet features a gourmet meal with appropriate wine.

This year, Lucien M. Pascucci, MD, will hand over the reins of the association's leadership to Stanley R. McCampbell, MD, who will become the 67th President since its incorporation in 1905.

Sporting events will be part of the 66th Annual Meeting when the association sponsors a golf and a tennis tournament. Plans for the golf tournament are still underway, but the tennis tournament will be held at the Will Rogers Memorial Tennis Center, 3400 N. Portland. It will start at noon on Friday, May 19th, with both singles and doubles events for men. Consolation rounds for the first round losers will be conducted and it is anticipated that a wives' tournament consisting of singles and doubles will be held. There is no entry fee and trophies will be awarded to the winners at the dinner-dance on Saturday evening. □

DISRS Issues Assignment Warning

Following in the steps of the Medicare Administration, Oklahoma's Department of Institutions, Social and Rehabilitative Services has issued a warning about physicians violating the assignment agreement on Medicare and Medicaid patients.

In a letter to all Oklahoma doctors L. E. Rader, Director of the Department, said "We have been advised by the Social Security Administration that the number of reported Medicare assignment violations, on a national basis, has shown a steady and significant increase in the past two years. Physicians and suppliers should make sure that their office staff or billing agents are thoroughly familiar with assignment provisions."

The OSMA has issued similar warnings to all Oklahoma physicians a number of times in the past. Under the law, acceptance of an assignment requires the physician to accept the carrier's determination of the allowable charge for a service as his full fee for that service. This means that the physician cannot bill the patient for any more than the difference between the allowable charge determined by the carrier and the payment received from the carrier. Payment cannot be demanded from the beneficiary in assignment cases for the difference between the allowable charge and the charge actually made by the physician, if a reduction of the actual charge has been made by the Medicare carrier.

Once a physician signs an assignment agreement it cannot be revoked in whole or in part by one party alone, without the consent of the other party. Even if the patient agrees to allow the physician to bill him for the difference, the physician cannot do so if he has taken the assignment.

Rader's letter went on to say, "In view of the increasing incidence of assignment violations, the Social Security Administration has asked for increased monitoring efforts by carriers. When possible assignment violation is indicated through carrier review, or on the basis of a beneficiary complaint, we will contact the physician or supplier to be sure that the provisions of the assignment agreement are understood by him and his office staff. *When a violation has occurred, assurances will be obtained that a refund or corrected bill will be sent to the beneficiary, and that beneficiaries will not be billed for reductions on assigned claims in the future.* If necessary, we are required to obtain the assistance of state or local medical societies or professional associations in securing discontinuance of assignment violations."

"Where, despite these efforts, there are repeated or uncorrected violations, we are required to suspend further payment to the physician or supplier on assigned claims," Rader said.

The OSMA policy is to encourage physicians not to accept assignment on Medicare cases. This alleviates the possibility that a physician might find himself violating federal law when he has accepted assignment.

On Medicaid patients, the acceptance of the assignment is automatic, since the state pays the physician directly except in very rare cases. A physician wishing to avoid assignment in the case of Medicaid is entitled to bill the patient directly, but he must bear in mind that he is dealing with an indigent. □

Pesticide Poisoning Data Published

Every spring, and then throughout the summer, Oklahoma physicians find themselves faced with an increasing number of pesticide poisoning cases. An article in the April 12th, 1971 issue of JAMA may offer some assistance.

Entitled "Analytical Diagnosis of Pesticide Poisoning" the article deals with the collection, storage, and shipment of biological samples for analysis.

Copies of the article are available through the Pesticides Program, Oklahoma State Department of Health, 3400 N. Eastern, Oklahoma City, Oklahoma 73105.

Persons desiring information on pesticide poisoning are encouraged to contact the program at Area Code 405, 427-1516 of 427-6561. □

New Telephone System For Medical Center

The University of Oklahoma Health Sciences Center, including University Hospitals, is scheduled to convert to a direct-in and direct-out dialing Centrex telephone system and to new telephone numbers around May 1st.

When the computerized electronic switching system goes into operation, callers will dial directly the department they wish instead of going through the switchboard. The present 236-1366 number for the entire center will be discontinued.

The number physicians should call if they do not know the individual department or party's number is 271-4000. All extensions will have four digits with the "271" prefix. □



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Plans Develop For Tulsa Medical School

A medical school in Tulsa, under the auspices of the University of Oklahoma, is about to become a reality. A consultant firm has completed a feasibility study which was presented to the Legislative Council, at a meeting in Tulsa on January 14th, 1972. The report, which is an updating of a previous study carried out in 1968, recommends the implementation of a plan developed recently and supported by the administration of the University of Oklahoma Health Sciences Center and the Tulsa Medical Education Foundation.

The plan, described as the "Y" plan, will:

1. Establish a clinical college of medicine in Tulsa as a part of the University of Oklahoma.

2. Gradually increase the size of the entering class of medical students from 150 to 200 students.

3. Accommodate all students for their first two years of the basic science curriculum in facilities of the College of Medicine in Oklahoma City.

4. Transfer the 50 new students to Tulsa for their last two years of clinical training, making a total enrollment in Tulsa of 100 students.

5. Get medical education underway in Tulsa many years sooner and at far less cost than would have been possible had a new free-standing medical school been undertaken.

The Executive Vice-President for Health Sciences Center Affairs of the University of Oklahoma has appointed a Search Committee for the Dean of the new school in Tulsa. The committee consists of:

Martin J. Fitzpatrick, MD, Professor of Medicine, Oklahoma City, Chairman

Jed Goldberg, MD, Assistant Clinical Professor of Gynecology and Obstetrics, Tulsa

James Hartsuck, MD, Assistant Professor of Surgery, Oklahoma City

Mark R. Johnson, MD, Associate Clinical Professor of Medicine, Oklahoma City

C. S. Lewis, Jr., MD, Past-President Tulsa County Medical Society, Assistant Clinical Professor of Medicine, Tulsa

Nelson Ordway, MD, Professor of Pediatrics, Oklahoma City

Wendell Smith, MD, President, Tulsa Medical Education Foundation, Tulsa

C. Thomas Thompson, MD, Clinical Associate in Surgery, Tulsa

The committee is at work. It solicits from any members of the profession in Oklahoma nominations and supporting information on physicians who may be qualified for consideration. Nominations should be directed to members of the committee or to Doctor Fitzpatrick at University of Oklahoma Health Sciences Center, P.O. Box 26901, Oklahoma City, Oklahoma 73190.

The dean will be selected from a final list of names submitted by the Search Committee. The Executive Vice-President will recommend his appointment by the Regents of the University through the President. The procedure follows that used for all major administrative appointments in the university.

The thoughtful consideration of qualified candidates by interested physicians will be very much appreciated. □

Doctors-Lawyers Plan Meeting

Members of the Joint Medical-Legal Relations Committee of the OSMA and the Oklahoma Bar Association are planning a two day institute for doctors and lawyers to be held at Arrowhead State Lodge on Lake Eufaula, July 21st-22nd.

Committee Co-Chairman Joe Glass, Tulsa Attorney, and Jack Richardson, MD, Tulsa orthopedic surgeon, announced that the program would cover such subjects as Malpractice Arbitration, Professional Corporations, The Uniform Consumer Credit Code, Food and Drug Administration Rules and Regulations, and a number of other topics of interest to both doctors and lawyers.

The Medical-Legal Institute is a joint project of the two associations and is held every two years. Registration fee for this year's institute will be $35, with no registration fee for attending spouses.

A formal program and registration material will be sent to all Oklahoma doctors and lawyers in late June. □

Cahill To Present Turner Lecture

George F. Cahill, Jr., MD, Professor of Medicine, Harvard University School of Medicine and Physician at Peter Bent Brigham Hospital, Boston, Massachusetts, will deliver the Second Annual Henry H. Turner Lecture in Endocrinology. His topic will be "Role of Insulin in Man."

The lecture will be given at 4 p.m., April 3rd, 1972 in the East and West Lecture Halls of the Basic Science Building, University of Oklahoma Health Sciences Center, Oklahoma City.

Doctor Cahill's lecture is the final of four Oklahoma Medical Research Foundation Lectures which were established last year by the Foundation's Board of Directors as a means of providing a valuable service to the practicing physicians of Oklahoma and to the staff of the O. U. Medical Center.

The Henry H. Turner Lecture in Endocrinology was established in 1970 as a means of honoring the late Doctor Turner, well-known Oklahoma City physician who completed 46 years of practice before his death in August, 1970.

Doctor Turner was recognized for his pioneer efforts in the use of radioisotopes, especially for diagnostic purposes. He lectured extensively throughout the world and medical textbooks describe a disorder called the "Turner Syndrome" which he identified and characterized. He was a Past-President of the Endocrine Society which he also served as secretary-treasurer for 25 years. He is one of only two persons honored by that society with a certificate of merit naming him "one of the world's most outstanding endocrinologists." □

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Drug Abuse Treatment Film Popular

A training film specifically designed to teach physicians how to handle drug abuse cases had been in the state of Oklahoma less than two days when requests began to come in for its use. The film was purchased by the OSMA and is entitled "What Did You Take?" It is available to all medical societies, hospital staffs, and other medical organizations interested in the care and treatment of the drug abusing patient.

Filmed at Beth Israel Medical Center in New York, the film acquaints physicians with the major signs and symptoms encountered in drug abuse. Also presented are the recommended methods of treatment and emergency management of the overdosed patient.

It was originally produced at the request of the New York State Department of Health to complement a booklet on drug abuse which they had published. The OSMA has published a similar book entitled "Drug Abuse Treatment Manual."

The film complements the OSMA manual which was compiled and published under the direction of Charles Smith, Jr., MD, Chairman of the OSMA Alcoholism and Drug Abuse Committee. Production of the manual was directed by two Oklahoma City psychiatrists with considerable experience in dealing with drug abusing patients, Jim Earls, MD, and Tom Donica, MD.

Anyone wishing to obtain copies of the manual or seeking a showing date for the new film should contact Ed Kelsay, Associate Executive Director of the Oklahoma State Medical Association.

"What Did You Take?" consists of 30 minutes of high intensity scenes in hospital emergency rooms and adjoining doctors' offices. They are the actual sights and sounds of emergency room action, since the film is of actual drug abuse emergencies.

The people in the film are not actors and it quickly becomes apparent that the film is for viewing by professional audiences only. It covers the emergency treatment of patients in the major classes of drug abuse—opiates, hallucinogens, sedatives and stimulants.

The OSMA's purchase of the film was made possible by a donation from the Hoffman-LaRoche Pharmaceutical Company. The donation came through the company's Roche Laboratory Division, Manufacturers of two of the most widely used items in the drug overdose treatment, the tranquilizers Librium and Valium. □

Roche Offers Professional Services

Roche Laboratories has established a special department of Professional Services which offers physicians immediate access to information. In addition they have established a number of medical emergency phone numbers for immediate pharmacological consultation.

Physicians and pharmacists are available 24 hours a day to handle emergency phone calls at Area Code 201, 235-2355. Specific information on pharmacological or product related consultation is available immediately.

Roche has also established a series of "Warm Lines" for immediate information on clinical management or drug crisis management.

Three warm lines each are available on amphetamines, hallucinogens, opiates and barbiturates. By dialing the number the physician receives a tape discussion regarding treatment modalities for the abused drug. Each discussion is conducted by a physician expert in the treating of a drug abusing patient. The telephone numbers are as follows:

Amphetamines: AC 312, 297-3170; Hallucinogens: AC 312, 297-3270; Opiates: AC 312, 297-4180; Barbiturtes: AC 312, 297-4280. (Although there are three numbers available on each substance, only the one nearest to Oklahoma is given here.)

Roche Laboratory also offers a film service and its film library contains a variety of medical films which are recommended for professional audiences only; *i.e.*, medical, nursing and allied scientific groups. To receive a catalog and arrange a film showing, you can contact a Roche sales representative or write to: Roche Film Library, c/o Association-Sterling Films, Inc., 600 Grand Avenue, Ridgefield, New Jersey 07657.

Among the other programs offered by the company is a "Indigent Patient Program" which insures that needy patients receive products from their physicians in private practice without cost. If a physician has a private patient who needs assistance, he can write the Department of Professional Services of Roche Laboratories, name the Roche product needed, and give a brief description of circumstances. It is not necessary to send the name and address of the patient. The drugs requested for the indigent patient will be promptly sent directly to the physician so that he may dispense them free of charge to the patient. □

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Pharmacists Report Decline in Amphetamines

A survey of pharmacists throughout the state of Oklahoma showed "heavy" decreases in amphetamine prescriptions since September 1st of last year.

Conducted at the request of Lucien M. Pascucci, MD, President of the OSMA, the survey resulted in 195 responses from pharmacists. One hundred fifty-nine described dramatic drops in amphetamine prescriptions.

In the survey letter to state pharmacists Pascucci said, "In August of last year, as President of the OSMA, I asked all Oklahoma physicians to voluntarily limit their prescribing of amphetamines and methamphetamines." He went on to ask the pharmacists to help him evaluate physician response by indicating whether or not there had been a slight, moderate, heavy, or no decrease in the prescribing of amphetamines.

Pharmacists from 61 Oklahoma counties responded, with 159 indicating a heavy decrease, 25 indicating a moderate decrease, 5 showed only a slight decrease, while 6 said there was no decrease in amphetamine prescriptions at all.

In a letter reporting the survey results to Governor David Hall, Doctor Pascucci said, "The results of this survey are most gratifying to me, personally." He closed by saying, "Since physicians are personally involved in combating drug abuse . . . we are the ones that must pick up the pieces and try to put them back together again . . . through our association we stand ready to assist you with your efforts in this regard. I believe that the results of this survey indicate that the physicians will respond."

In a letter to all members of the association last August Doctor Pascucci had urged Oklahoma physicians to voluntarily place an almost total ban on the prescribing of amphetamines and methamphetamines except in those cases where they are the drug of choice. This would include cases of narcolepsy and selected cases of hyperactive and brain damaged children.

The results of the survey indicate that the president's plea was honored almost immediately. One pharmacist reported that amphetamine prescriptions dropped to nearly nothing before September 1st.

Of the 32 pharmacists in the Oklahoma City area responding to the survey, 24 indicated a heavy decrease in amphetamine prescriptions, four showed a moderate decrease, two a slight decrease, and two indicated no decrease at all. Ten Tulsa pharmacists responded, with six showing a heavy decrease, two a moderate decrease, and two a slight decrease.

Pharmacists reported similar results from Muskogee, McAlester, Lawton, Altus, Enid, Ponca City, and approximately 75 other Oklahoma communities.

In commenting on the survey results, Doctor Pascucci said, "The medical profession throughout the state is to be congratulated on this effort to police itself. . . . our members have responded enthusiastically to this assault on the drug abuse problem." He went on to take the opportunity to again urge all physicians to continue the ban on prescribing of amphetamines and methamphetamines. He stressed that it is important for physicians to reassess their prescribing of drugs with abuse potential and to insure that the profession does not inadvertently contribute to drug dependence. □

DEATH

COLIN M. MacLEOD, MD
1910-1972

President of the Oklahoma Medical Research Foundation, Colin M. MacLeod, MD, died in London, England, February 12th, 1972. One of the pioneers in heredity research, Doctor MacLeod was considered one of the most knowledgeable Americans in the field of microbiology.

A native of Post Hastings, Novia Scotia, Doctor MacLeod received his medical degree from McGill University Faculty of Medicine in 1932. He held several teaching positions in various medical centers in the United States before coming to the Oklahoma Medical Research Foundation.

He was a member of the National Academy of Sciences, a charter member of the Institute on Medicine, served as deputy director of the Office of Science and Technology at the White House from 1963-1966. Since 1965, he had served as chairman of the U.S. Delegation, U.S.-Japan Cooperative program in the Medical Sciences and was chairman of the technical committee to the Pakistan-SEATO Cholera Research Laboratory in Dacca.

Doctor MacLeod served the medical profession for 40 years in a career which brought him much acclaim and many honors. □

Book Reviews

I. TASTE AND SMELL IN VERTEBRATES: A CIBA FOUNDATION SYMPOSIUM. Edited by G. E. W. Wolstenholme and Julie Knight. First Edition, hard cover, 402 pp., with 163 illustrations, 104 Gloucester Place, London: J. A. Churchill, 1970.

This volume contains the proceedings of the Fifth CIBA Symposium on sensory functions in vertebrates, specifically dealing with taste and olfaction, and brings together in a single source a large body of recent information related to these topics.

Chapters concerning the taste function deal with the anatomy and physiology of taste endings, physiological and behavioral processes, properties of taste receptors, neural and perceptual responses to taste stimuli, effects of circulation, and taste specificity problems. Dealing with olfaction are chapters which include: The olfactory surface and bulb,

(Continued on Page xxix)

(Continued from Page 126)
the structure of olfactory receptors, olfaction in mammals, recent developments in "penetration and puncture" theory, computer correlation of molecular shape with odor, the higher olfactory centers, structurally unrelated odorants, and experiments in olfaction.

Each chapter in the text is followed by a concise summary and by a critical discussion by symposium participants. The text is clear and the illustrations are profuse and lucid. For those interested in this area, the book offers an authoritative, stimulating, and remarkably complete exposition of present understandings of the taste and olfactory functions. —*Donald T. Counihan, PhD*

JUVENILE RHEUMATOID ARTHRITIS. MAJOR PROBLEMS AND CLINICAL PEDIATRICS. Volume 6. By Earl J. Bore., Jr., MD. 231 pp. Philadelphia: W. B. Saunders Company. 1970. $12.50.

This is a clinically oriented monograph which discusses all aspects of juvenile rheumatoid disease. It focuses on the patient throughout and relates all information to the recognition, diagnosis and management of the child with this disorder. The first five chapters review the clinical manifestations, laboratory findings and differential diagnoses in a comprehensive manner. This is followed by a chapter on the psychological aspects of the disorder and an extensive, well-illustrated section on the home care of the child with rheumatoid disease. The final chapters deal with the orthopedic management and drug therapy.

All persons concerned with children and with this disorder will find this book of interest.—*Harris D. Riley, Jr., M.D.*

THE FROZEN CELL — A CIBA FOUNDATION SYMPOSIUM. Edited by G. E. W. Wolstenholme, and Maeve O'Connor, 316 pp.

There is considerable interest from the scientific point of view in the prolonged preservation of biological specimens. The symposium helps delineate the scientific basis for freezing of cells. It discusses the precise effects of different freezing or cooling procedures in different concentrations of protective compounds on physical parameters and biological systems. It is clear that the mechanism of freezing injury or conversely the mechanism of prevention of cellular injury by partial or total non-aqueous environment is not yet understood. The most practical progress has been in the area of blood banking. Investigators and blood bank directors who are contemplating initiating various types of cells storage will find these proceedings to be of value. The symposium deals with topics in too detailed a manner to be useful as a source of general information.—*Harris D. Riley, Jr., MD*

MUTATION AS CELLULAR PROCESS. Edited by G. E. W. Wolstenholme and Maeve O'Connor, CIBA Foundation, Meeting Chairman, R. F. Kimball, Biology Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee, U.S.A. Hard Cover, 244 pp. with 48 illustrations. London, J & A Churchill Ltd., 1969.

This symposium, which was held in England in February of 1969, is another in the series of excellent symposia sponsored by the CIBA Foundation. The emphasis of this symposium was on the biological events which follow the initial action of mutagens and which lead to biological expression of the mutation. This is in contrast to the large amount of attention given to the direct molecular changes which occur in DNA as a result of the action of mutagens and to the repair of defective DNA by enzymes of the cell. Most of the work reported deals with studies which were made with bacteriophage, bacteria and yeast and is of a theoretical nature. Unfortunately, the book was received for review only recently and some of the material is now dated. As usual, the calibre of the speakers and the presentation of the material is up to the high standards established for this series.—*John Sokatch, PhD*

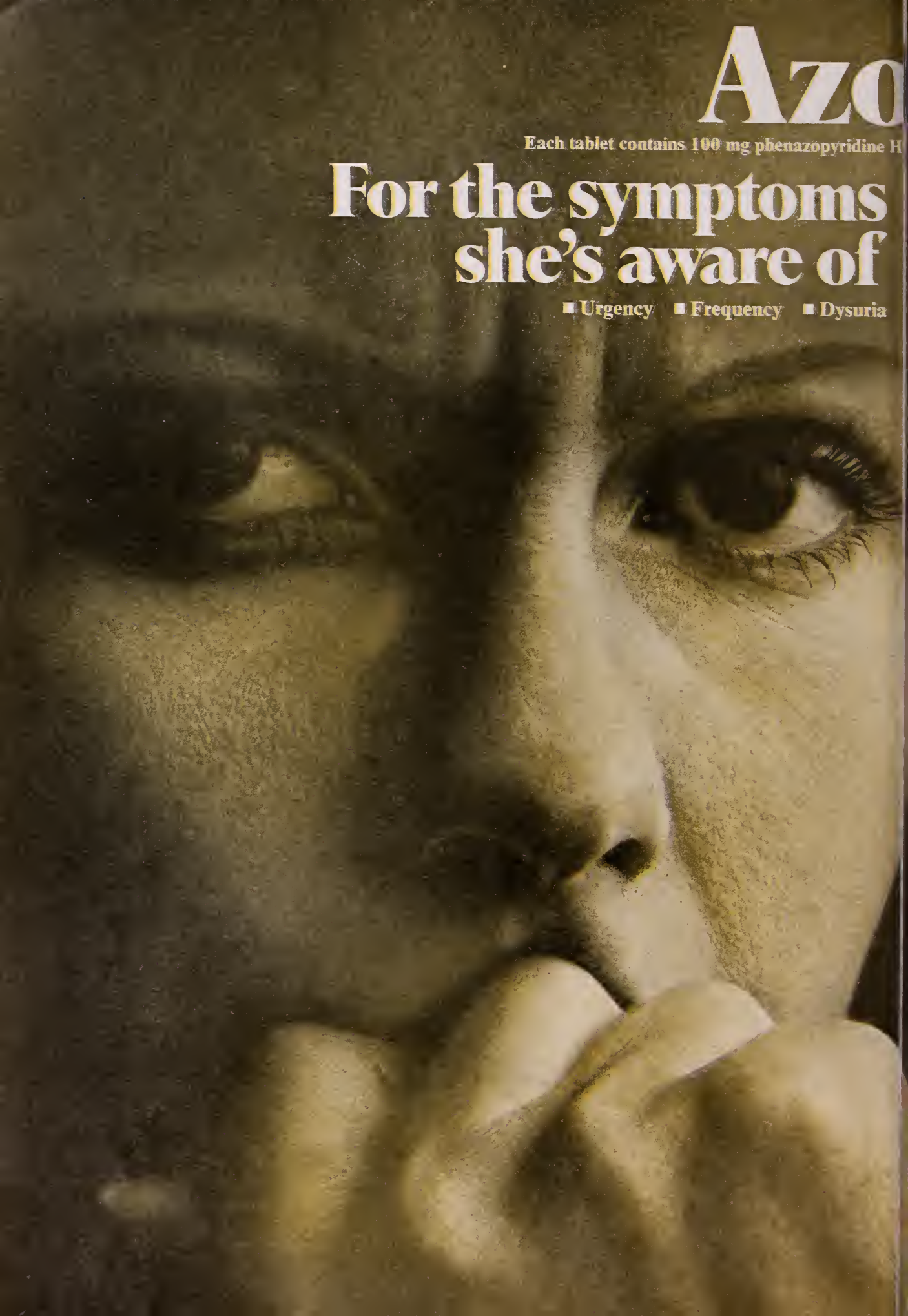
CIBA FOUNDATION: FOETAL AUTONOMY. Edited by G. E. W. Wolstenholme and Maeve O'Connor. First published 1969 with 73 illustrations. J. & A. Churchill, Ltd., 1969.

As G. S. Dawes states in his opening remarks, there are wide gaps between the different disciplines that study and publish on fetal anatomy and function. The symposium attempted to "spot the connexions between the different branches of the subject." This volume is well organized, following the natural progression of the conceptus from embryo, to fetus, to perinatal life. Considerable emphasis is on animal experimentation which has been the chairman's forte. Most of the articles synthesize current research into easily understandable structures, but it is the completely reported discussions that make this volume so valuable. Both obstetricians and pediatricians would profit from the sections on fetal endocrine autonomy and the fetal role in parurition. Professor Jost gives a lucid description of his life's work. The innovative experiments of Liggins are well discussed, especially with its suggestions on control of fetal lung development. Overall it is fortunate that the English have not yet yielded to the temptation of publishing only excerpts from discussions of symposia. This satisfies more physicians because each physician finds interest in slightly different objects, what one finds exciting, another sees as dull. The book is valuable because it holds the reader's interest.—*Robert V. Kotas, MD*

BIOLOGY AND THE FUTURE OF MAN. Edited by Phillip Handler. New York: Oxford University Press, 1970. 936 pp. $12.50.

Several years ago the Committee on Science and Public Policy of the National Academy of Sciences embarked upon a series of surveys of the scientific disciplines. Each survey was to begin with an appraisal of the "state of the art" in a given discipline, namely a summary of the progress which has been made recently in approaching the major

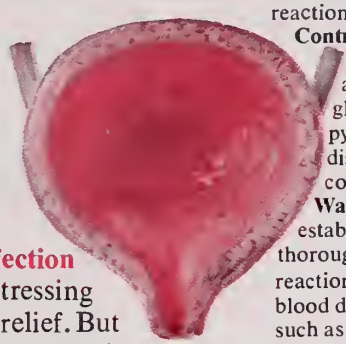
(Continued on Page xxxii)


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Indications: In adults, urinary tract infections complicated by pain (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli, Klebsiella-Aerobacter, Staphylococcus aureus, Proteus mirabilis,* and, less frequently, *Proteus vulgaris*) in the absence of obstructive uropathy or foreign bodies. *Important Note:* Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response. Add aminobenzoic acid to culture media for patients already taking sulfonamides. Increasing frequency of resistant organisms currently is a limitation of the usefulness of antibacterial agents. Blood levels should be measured in patients receiving sulfonamides for serious infections, since there may be wide variations with identical doses; 12 to 15 mg/100 ml is considered optimal for serious infections; 20 mg/100 ml should be the maximum total sulfonamide level, as adverse reactions occur more frequently above this level.

Contraindications: Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period. Contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with gastrointestinal disturbances, because of phenazopyridine HCl component.

Warnings: Safe use in pregnancy has not been established, and teratogenicity potential has not been thoroughly investigated. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported; clinical signs such as sore throat, fever, pallor, purpura or jaundice may be early indications of serious blood disorders. Complete blood counts and urinalysis with careful microscopic examination should be performed frequently during sulfonamide therapy.

Precautions: Use with caution in patients with impaired renal or hepatic function, severe allergy, bronchial asthma and in glucose-6-phosphate dehydrogenase-deficient individuals. In the latter, hemolysis, a frequently dose-related reaction, may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias:* agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia; *allergic reactions:* erythema multiforme (Stevens-Johnson syndrome), skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis; *gastrointestinal reactions:* nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis; *C.N.S. reactions:* headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia; and *miscellaneous reactions:* drug fever, chills, toxic nephrosis with oliguria and anuria, polyarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide and thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

Dosage: Usual adult dosage for acute, painful phase of urinary tract infection is 4 tablets initially, then 2 tablets morning and evening. If pain persists beyond seven days, causes other than infection should be sought. After relief has been obtained, continued treatment with Gantanol (sulfamethoxazole) may be considered.

NOTE: Patients should be told that the orange-red dye (phenazopyridine HCl) will color the urine soon after ingestion.

How Supplied: Tablets, each containing 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl, bottles of 100 and 500.

(Continued from Page xxix)

outstanding questions in that discipline. In addition the survey was to assess the nature and strength of our national apparatus for continuing attack on major problems. Finally, each survey was to undertake a projection of future needs for national support of the discipline in question to assure that our national effort in this regard is optimally productive within the framework of the sources which could reasonably be brought to bear. Reports of such surveys have been published in the fields of chemistry, physics, ground-based astronomy, mathematics and computer science. In 1966, the Academy determined that there was a compelling need for an equivalent survey of the life sciences. This book is the culmination of that effort.

In preparation for nearly four years, it represents the combined work of about 200 biologists. It has been edited by Phillip Handler, President of the National Academy of Sciences. To keep the price down considering that the book is over 900 pages in length and is packed with charts, diagrams and photographs, the authors have waived all royalties.

Beginning with the origin of life and ending with the role of biology in the future of human society, the study brings together in a single volume the reports of 21 scientific panels made up of authorities in various disciplines. Starting at the molecular level, the book offers a logical intellectual structure for the life sciences dealing in turn with subcellular organelles, cells, tissues and organs, organisms, species and ecological systems. The enormous scope of the book is indicated by its chapter headings which include: Molecular Biology, the Materials of Life and Their Transformation, Cells, the Units of Life, the Origins of Life, the Biology of Development, the Functions of Tissues and Organs, Biological Structures — from Molecules to Man, the Nervous System, the Biology of Behavior, What is Ecology?, Heredity and Evolution, the Diversity of Life, Digital Computers in the Life Sciences, On Feeding Mankind, Science and Medical Practice, Renewable Resources, Biology and Industrial Technology, Environmental Health and Biology and the Future of Man.

It is possible only to give certain general impressions and themes of this monumental work. The broad focus of the book is on ways of using our knowledge of living phenomenon for humanity benefit in agricultural and medical practice, in industry, in environmental health and in the renewal of resources. It deals in large measures with the fundamental question, "What has been happening to our environment and what can be done to reverse the trend?" It is clear that these reports are in a sense an acknowledgement of the debt American science owes to public support and points out the effects of reduction in federal financing for research.

In general the writing is excellent. *Biology and the Future of Man* is not merely a book. It is an opportunity to learn about what is perhaps the most interesting and exciting contemporary scientific disciplines from the men who have worked with them and who have offered their knowledge in a form that is exceptionally well suited to inform the public.

This book represents a major contribution to human biology, and although it is diverse and highly technical in places, it is strongly recommended. The chief defect of the book is the absence of an index, the inclusion of which would enhance its usefulness substantially.—*Harris D. Riley, Jr., MD*

BRITISH MEDICAL BULLETIN, Volume 27, Number 1, 1971. "Epidemiology of Non-Communicable Disease." Edited by E. D. Acheson, London, The British Council, 1971, 94 pp.

This volume of the *British Medical Journal* is concerned with the epidemiology of non-communicable disease and is of the usual high standards which readers have come to associate with this journal. Cochrane and Holland in the first article discuss the ethics of screening programs. They conclude that the physician should have conclusive evidence that screening can alter the natural history of disease in a significant portion of those screened before undertaking extensive programs. Colley provides an excellent survey of respiratory disease in childhood. There are two important articles on epidemiology of cancer; Cook and Burkitt discuss neoplastic disease on the African Continent, and Stewart and Barber provide an excellent summary of the epidemiologic importance of childhood cancers. Two particularly interesting chapters are those entitled "Epidemics of Rare Diseases" by Knox and that by McKeown and Record on "Environmental Influences on Development of Intelligence."

A commendable feature of the symposium is the conciseness of the contributions. Despite the shortness, they are packed with valuable information. *Harris D. Riley, Jr., M.D.*

PEDIATRIC HEMATOLOGY. By Alvin M. Mauer, MD. 486 pp. New York: McGraw-Hill Book Company, 1969. $23.00.

This book is clearly written and the references are well chosen and extend the value of the book beyond that of the usual single-authored text which often substitutes author opinion for literature. The author, an experienced pediatric hematologist at the Children's Hospital of Cincinnati, has provided an excellent text in this important area of medicine.

Although generally of high order, there are certain deficiencies. Although the section on intrauterine transfusion contains adequate detail, the book was published shortly before an analysis of phototherapy of neonatal jaundice could be included. The section on susceptibility to infection is somewhat brief. Readers will find the section on therapy of leukemia particularly revealing.

This book is highly recommended for students, house officers, fellows and physicians in practice. It is a welcome addition. *Harris D. Riley, Jr., M.D.*

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1.2 to 8 grams/day IV dosage range: Most hospitalized patients with uncomplicated pneumonias respond satisfactorily to 1.2 to 1.8 grams/day of Lincocin IV. These doses may have to be increased for more serious infections. In life-threatening situations as much as 8 grams/day has been administered intravenously to adults.

In usual IV doses, Lincocin (lincomyci hydrochloride, Upjohn) should be diluted in 250 ml or more of normal saline solution or 5% glucose in water. But when 4 grams or more per day is given, Lincocin should be diluted in nc less than 500 ml of either solution, and the rate of administration should not exceed 100 ml/hour. Too rapid intravenous administration of doses exceeding 4 grams may result in hypotension or, in rare instances, cardiopulmonary arrest.

Effective gram-positive antibiotic: Lincocin IV is effective in respiratory tract, skin and soft-tissue, and bone

nfections caused by susceptible strains of pneumococci, streptococci, and staphylococci, including penicillin-resistant strains. Staphylococcal strains resistant to Lincocin (lincomycin hydrochloride, Upjohn) have been recovered. Before initiating therapy, culture and susceptibility studies should be performed. Lincocin has proved valuable in treating patients hypersensitive to penicillin or cephalosporins, since Lincocin does not share antigenicity with these compounds. However, hypersensitivity reactions have been reported, some of these in patients known to be sensitive to penicillin.

Well tolerated at infusion site: Lincocin intravenous infusions have not produced local irritation or phlebitis, when given as recommended. Lincocin is usually well tolerated in patients who are hypersensitive to other drugs. Nevertheless, Lincocin should be used cautiously in patients with asthma or significant allergies.

In patients with impaired renal function, the recommended dose of Lincocin should be reduced to 25–30% of the dose for patients with normal kidney function. Its safety in pregnant patients and in infants less than one month of age has not been established.

Lincocin may be used with other antimicrobial agents: Since Lincocin is stable over a wide pH range, it is suitable for incorporation in intravenous infusions; it also may be administered concomitantly with other antimicrobial agents when indicated. However, Lincocin should not be used with erythromycin, as *in vitro* antagonism has been reported.

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Sterile Solution (300 mg per ml)

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Each preparation contains:	Lincomycin hydrochloride monohydrate equivalent to lincomycin base
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Syrup per 5 ml	250 mg

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Lincocin (lincomycin hydrochloride) is indicated in infections due to susceptible strains of staphylococci, pneumococci, and streptococci. *In vitro* susceptibility studies should be performed. Cross resistance has not been demonstrated with penicillin, ampicillin, cephalosporins, chloramphenicol or the tetracyclines. Some cross resistance with erythromycin has been reported. Studies indicate that Lincocin does not share antigenicity with penicillin compounds.

CONTRAINDICATIONS: History of prior hypersensitivity to lincomycin or clindamycin. Not indicated in the treatment of viral or minor bacterial infections.

WARNINGS: *CASES OF SEVERE AND PERSISTENT DIARRHEA HAVE BEEN REPORTED AND HAVE AT TIMES NECESSITATED DISCONTINUANCE OF THE DRUG. THIS DIARRHEA HAS BEEN OCCASIONALLY ASSOCIATED WITH BLOOD AND MUCUS IN THE STOOLS AND HAS AT TIMES RESULTED IN AN ACUTE COLITIS. THIS SIDE EFFECT USUALLY HAS BEEN ASSOCIATED WITH THE ORAL DOSAGE FORM BUT OCCASIONALLY HAS BEEN REPORTED FOLLOWING PARENTERAL THERAPY.* A careful inquiry should be made concerning previous sensitivities to drugs or other allergens. Safety for use in pregnancy has not been established and Lincocin (lincomycin hydrochloride) is not indicated in the newborn. Reduce dose 25 to 30% in patients with severe impairment of renal function.

PRECAUTIONS: Like any drug, Lincocin should be used with caution in patients having a history of asthma or significant allergies. Overgrowth of nonsusceptible organisms, particularly yeasts, may occur and require appropriate measures. Patients with pre-existing monilial infections requiring Lincocin therapy should be given concomitant antimonilial treatment. During prolonged Lincocin therapy, periodic liver function studies and blood counts should be performed. Not recommended (inadequate data) in patients with pre-existing liver disease unless special clinical circumstances indicate. Continue treatment of β-hemolytic streptococci infections for 10 days to diminish likelihood of rheumatic fever or glomerulonephritis.

ADVERSE REACTIONS: *Gastrointestinal*—Glossitis, stomatitis, nausea, vomiting. Persistent diarrhea, enterocolitis, and pruritus ani. *Hemopoietic*—Neutropenia, leukopenia, agranulocytosis, and thrombocytopenic purpura have been reported. *Hypersensitivity reactions*—Hypersensitivity reactions such as angioneurotic edema, serum sickness, and anaphylaxis have been reported, sometimes in patients sensitive to penicillin. If allergic reaction occurs, discontinue drug. Have epinephrine, corticosteroids, and antihistamines available for emergency treatment. *Skin and mucous membranes*—Skin rashes, urticaria, vaginitis, and rare instances of exfoliative and vesiculobullous dermatitis have been reported. *Liver*—Although no direct relationship to liver dysfunction is established, jaundice and abnormal liver function tests (particularly serum transaminase) have been observed in a few instances. *Cardiovascular*—Instances of hypotension following parenteral administration have been reported, particularly after too rapid IV administration. Rare instances of cardiopulmonary arrest have been reported after too rapid IV administration. If 4.0 grams or more administered IV, dilute in 500 ml of fluid and administer no faster than 100 ml per hour. *Special senses*—Tinnitus and vertigo have been reported occasionally. *Local reactions*—Excellent local tolerance demonstrated to intramuscularly administered Lincocin (lincomycin hydrochloride). Reports of pain following injection have been infrequent. Intravenous administration of Lincocin in 250 to 500 ml of 5% glucose in distilled water or normal saline has produced no local irritation or phlebitis.

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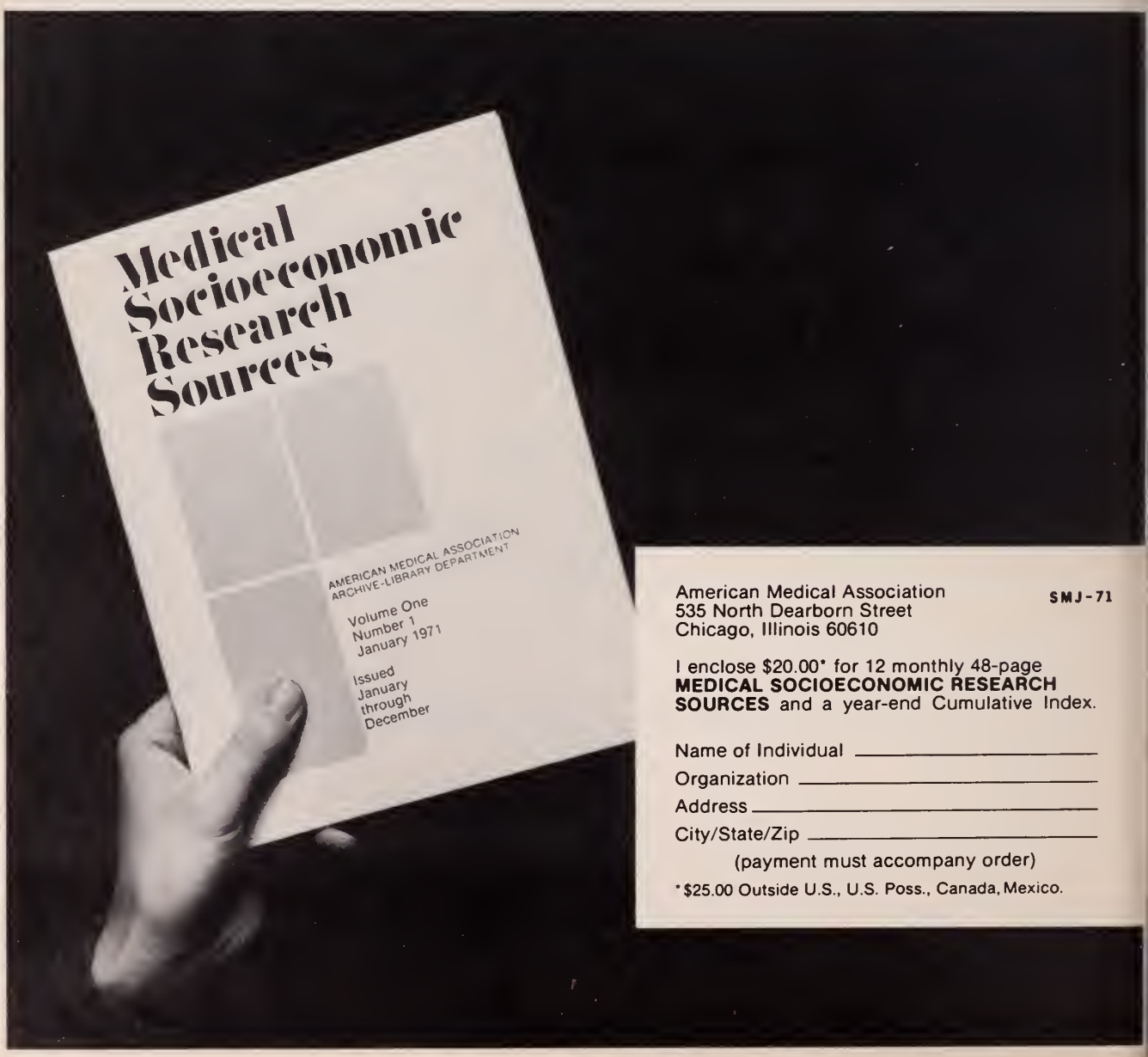
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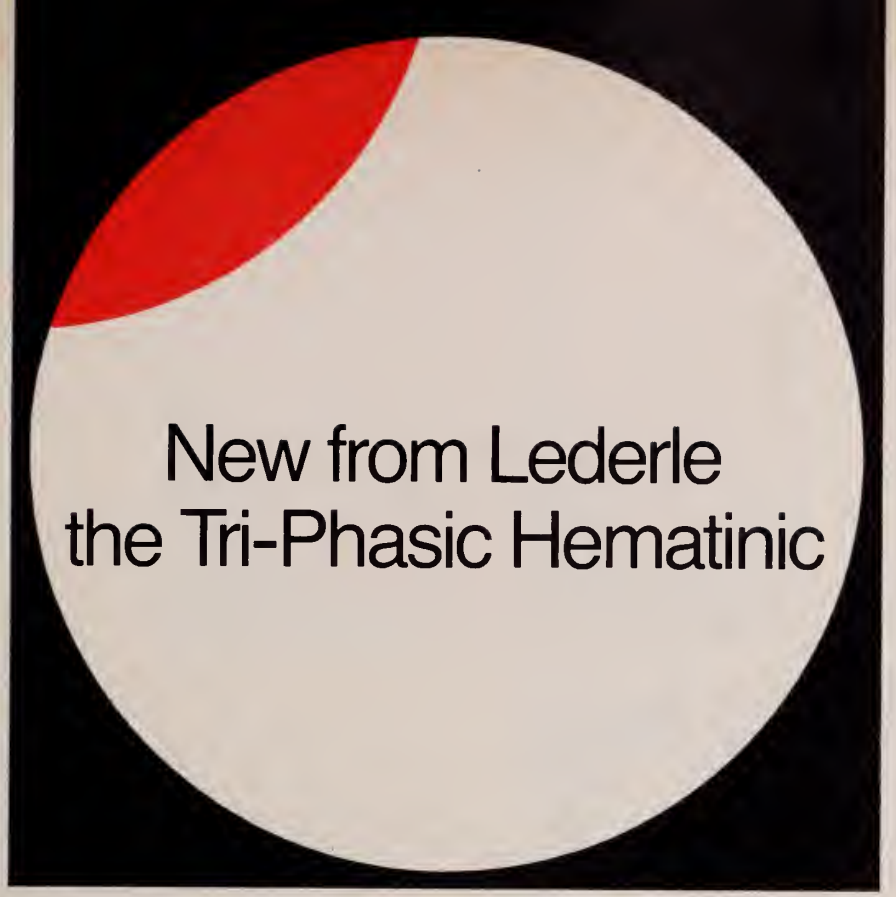
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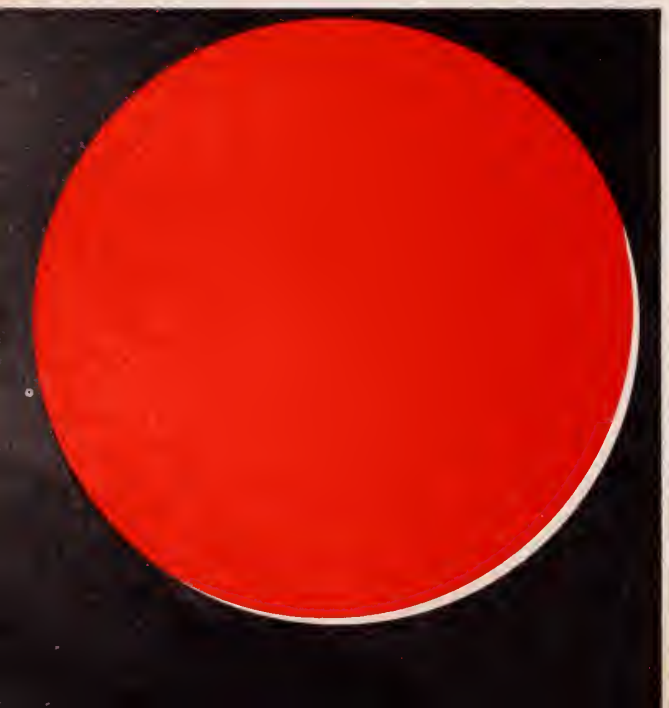
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Adverse Reactions: G.I.: nausea, vomiting, diarrhea, abdominal pain. Skin rashes may occur. Such reactions may necessitate temporary or permanent changes in dosage or usage. Allergic sensitization has been reported following both oral and parenteral administration of folic acid.

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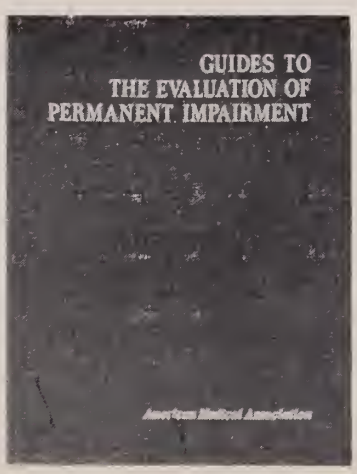
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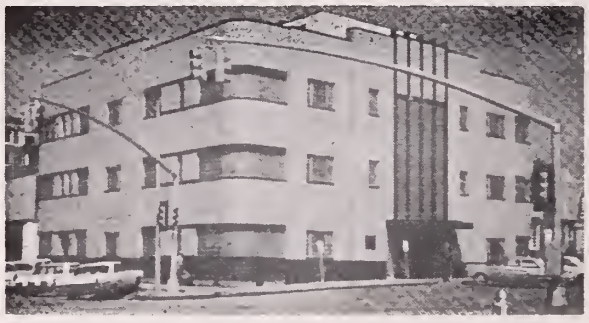
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The JOURNAL *of the Oklahoma State Medical Association*

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News Copy, Miscellaneous Ads ..... July 1, 1972

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NEWS

Members of the Oklahoma State Medical Association, the constituent societies of the association, and all readers in general are invited to supply news items of general interest to the profession.

ADVERTISING

All advertising copy must be approved by the Editorial Board before acceptance for publication. General and miscellaneous advertising rates will be sent on request.

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Authors will receive reprint order forms from the Transcript Press, P.O. Drawer 1058, Norman, Oklahoma 73069, prior to final publication of their articles. Other requests for reprints must be made to the Transcript Press within 30 days after publication.

BACK ISSUES

Microfilm copies of back issues of *The Journal* may now be purchased from University Microfilms, 300 North Zeeb Road, Ann Arbor, Michigan 48106.

HEALTH EDUCATION AND VOLUNTEER SERVICES

Two *new* national committees were appointed for 1971-72—*Health Education and Volunteer Health Services*—and they will work together to coordinate your community health activities.

The Health Education committee will provide educational materials for all your committees. The Volunteer Services committee will help you put these materials into action.

Under the present state and county auxiliary structure, there are several chairmen relating to one national chairman. Under the Health Education this could include health education (education of teachers, parents, teenagers and the public), mental health, safety, environmental health, community health, rural health and would cover such areas as immunization, nutrition, physical fitness, family planning and health frauds and quackery.

This committee will assist you with using package programs and other materials developed by the national auxiliary and the AMA. New materials will be developed as needed, or requested.

Your Health Education committee will work with all state and county committees, helping with the selecting of the best materials for educating the public, whatever the health concern might be.

The Volunteer Health Services committee will promote and devise action programs to meet specific community health needs. It will put your volunteers into action!

The chairmen working under this national committee might include: community service; children and youth (including special services); Block Mother Plan; GEMS; homemaker services; meals services; mental health nutrition; safety and the blood donor program.

These chairmen would report the materials used to the national Health Education chairman and the type of action programs to the national Volunteer Health Services chairman. A "double" report form will be furnished for this purpose.

As an example of how these two new committees can work together, let us focus on our No. 1 concern—"Drug Abuse."

Last year every state auxiliary reported county programs and projects on drug abuse.

In Nebraska, where a health education committee is working effectively, the auxiliary co-sponsors, with the medical society and educational television, a series of programs. Every Monday night in January programs were shown on "Drugs, Use and Abuse."

In East Baton Rouge, Louisiana, the auxiliary sponsored a particularly intensive project, involving many in the community. It sponsored a work-shop for 50 volunteer physicians; purchased films to be used in the program and loaned to other groups; sponsored a "Drug Alert Week" with an outstanding guest speaker.

The Louisiana-type project would be coordinated by the Volunteer Health Services committee, using the brochures, films, speeches, scripts and other educational materials provided by the Health Education committee.

A Health Education Committee working with a Volunteer Health Services Committee coordinating your auxiliary activities in the fight against drug abuse can do much to make you leaders in health.

A Drug Abuse Program is only one of the many areas where your auxiliary can provide leadership for the community as a whole. Other areas in Oklahoma where auxiliaries can provide excellent leadership and also the needed package programs we have available to us are: Alcohol, Block Mother Plan, Health Manpower, Immunization, Sex Education, Smoking, Teenage Venereal Disease and Physical Fitness, Mental Health for Children, Homemaker Services, Blood Donor Programs and GEMS.

Write to auxiliary headquarters, 535 North Dearborn Street, Chicago, Illinois 60610, for a copy of any program your auxiliary wishes to use.

Always remember, before your auxiliary embarks on any NEW PROJECT, you must obtain the approval of your County Medical Society. They will usually not only give their approval but will usually also give much needed assistance. □

OSMA JOURNAL / *the last word*

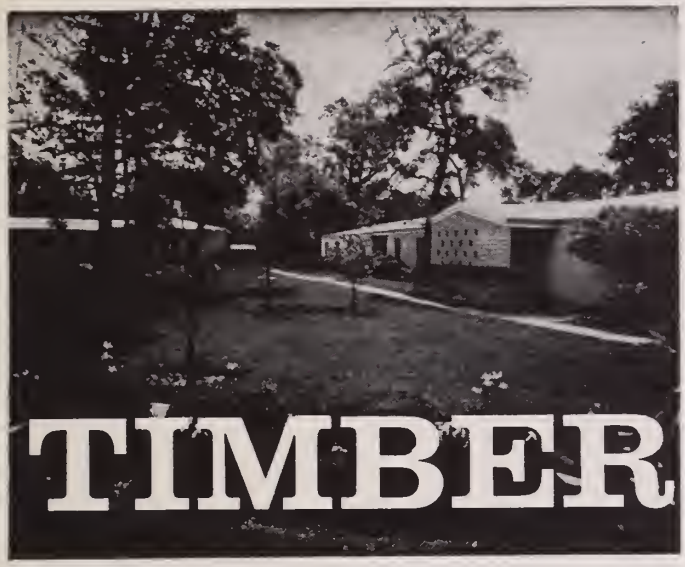
A new phase "contract practice" is being used to describe some of the health care delivery programs being advocated, in particular health maintenance organizations. In testimony before the U. S. Senate Finance Committee the AMA urged that any type of contract practice should be thoroughly tested through controlled demonstrations before any attempt is made to initiate nationwide coverage for Medicare beneficiaries. It pointed out that under one proposed amendment the government would increase its financial support under Medicaid only when services are provided in a government contract practice or a community center. Such an approach the AMA said, would tend to destroy the patient's choice of medical care and could lead states to require that medical care under Medicaid be furnished only in "favored settings" so the states could capitalize on additional federal funding.

A major publicity campaign has been launched by the American Chiropractic Association. Capitalizing on the drug abuse theme, the program calls for the substitution of chiropractic services for all pharmaceuticals. The goal of the campaign is made clear in the instructions on the use of the kit sent to state chiropractic groups—"an anti-drug approach is more beneficial and meaningful to chiropractic than any other health profession, because doctors of chiropractic do not prescribe drugs." Materials for the campaign include speeches, news releases, radio and television service spots, newspaper ads, bumper stickers, billboard posters and a pamphlet. The ads and posters say such things as "Don't be a pill popper" and "Protect Your Health With Spinal Care." The ACA says its program "gives credence to chiropractics' authority on matters governed by the spine, **which includes all functions of the body."**

The so-called health care crisis exists . . . apparently for other people. A recently released study by the University of Chicago's Center for Health Administration Studies revealed that the "crisis" may be more illusionary than real. More than 3,200 families, representing a nationwide sample, were interviewed by the center. When asked if they thought there is a crisis in health care today in the U.S., 76 percent of the respondents said "yes." But when asked whether they were dissatisfied with the quality of their own health care, only ten percent answered "yes." Apparently most people feel that there is a crisis—for others but not for themselves. Only 13 percent of the families felt it was not easy or convenient to get a doctor, but 43 percent expressed dissatisfaction with the availability of medical care at night and on weekends.

Continuing medical education is a fact of life in Oregon. In January that state's medical society suspended eleven MDs who failed to keep their education up to date. The Oregon Medical Association requires its members to take the equivalent of 50 hours a year of formal continuing medical education. Suspended members are allowed back in the organization when they show they have, in fact, met the requirement or, they can wait a year and rejoin the association as new members.

In his book "1984" George Orwell described a mental process called "double think." This was where you proved a theory by presenting evidence to the contrary. Senator Edmund Muskie performed this type of mental gymnastics in a recent news release when he said, "I have seen, as you have, over-crowded hospital corridors and overworked doctors and nurses. They stand as bleek testimony to the failure of a medical care system that is in fact a system of medical neglect." The comment was made to support Muskie's proposal for a massive drive to create health maintenance organizations. The news release said "a person pays one sum to the HMO and then, during the year, the HMO **treats all that individual's medical needs."** It looks like double think at its best to say that you can correct overcrowded hospital corridors and overworked doctors and nurses by giving away medical care. □



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Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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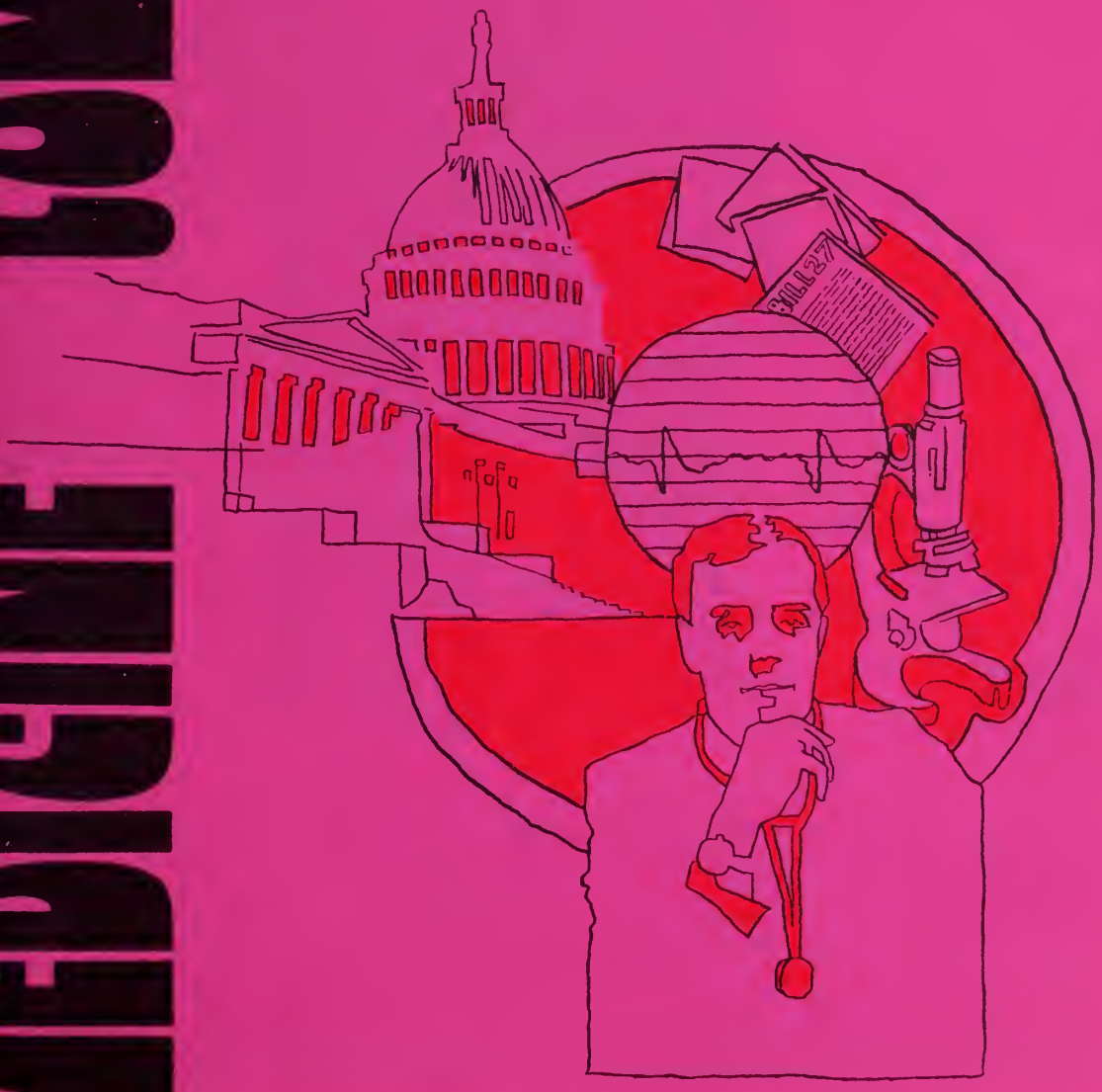
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Volume 65—Number 4—April 1972

BALCONY

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ANNOUNCING THE 1972 OSMA ANNUAL MEETING



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Contraindications: History of hypersensitivity to thiabendazole.
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For more detailed information, consult your MSD representative or see the Direction Circular. Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa. 19486

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addendum

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Threadworm,* large roundworm,* hookworm,* and whipworm* disease	Two doses of 1 tablet/50 lb	Repeat the next day	Alternatively, a single dose of 2 tablets/50 lb may be given. However, a higher incidence of side effects should be expected.
Creeping eruption	Two doses of 1 tablet/50 lb	Repeat the next day	If active lesions are still present 2 days after completing this regimen, a second course is recommended.
Symptoms of trichinosis* during the invasive phase of the disease	Two doses of 1 tablet/50 lb	Repeat for 2 to 4 successive days	The optimal dosage for the treatment of trichinosis has not been established.

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*Clinical experience with thiabendazole for treatment of each of these conditions in children weighing less than 30 lb has been limited.

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Arthur los



A single-dose, non-staining anthelmint

his pinworms...



with just one non-staining dose of Antiminth (pyrantel pamoate) Oral Suspension.

Highly effective. Active against pinworm...and roundworm.

Non-staining. Doesn't stain teeth or oral mucosa on ingestion. Doesn't stain stools, clothing or linen.

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Well-tolerated. Based on pre-introductory studies.

Pleasant-tasting. Easy-to-take, caramel-flavored oral suspension.

Economical. One prescription for the entire family.

Antiminth (pyrantel pamoate) Oral Suspension

Actions. Antiminth (pyrantel pamoate) has demonstrated anthelmintic activity against *Enterobius vermicularis* (pinworm) and *Ascaris lumbricoides* (roundworm). The anthelmintic action is probably due to the neuromuscular blocking property of the drug.

Antiminth is partially absorbed after an oral dose. Plasma levels of unchanged drug are low. Peak levels (0.05-0.13 μg/ml) are reached in 1-3 hours. Quantities greater than 50% of administered drug are excreted in feces as the unchanged form, whereas only 7% or less of the dose is found in urine as the unchanged form of the drug and its metabolites.

Indications. For the treatment of ascariasis (roundworm infection) and enterobiasis (pinworm infection).

Warnings. *Usage in Pregnancy:* Reproduction studies have been performed in animals and there was no evidence of propensity for harm to the fetus. The relevance to the human is not known.

There is no experience in pregnant women who have received this drug.

Precautions. Minor transient elevations of SGOT have occurred in a small percentage of patients. Therefore, this drug should be used with caution in patients with pre-existing liver dysfunction.

Adverse Reactions. The most frequently encountered adverse reactions are related to the gastrointestinal system.

Gastrointestinal and hepatic reactions: anorexia, nausea, vomiting, gastralgia, abdominal cramps, diarrhea and tenesmus, transient elevation of SGOT.

CNS reactions: headache, dizziness, drowsiness, and insomnia.

Skin reactions: rashes.

Dosage and Administration. *Children and Adults:* Antiminth Oral Suspension (50 mg. of pyrantel base/ml.) should be administered in a single dose of 11 mg. of pyrantel base per kg. of body weight (or 5 mg./lb.); maximum total dose 1 gram. This corresponds to a simplified dosage regimen of 1 cc. of Antiminth per 10 lbs. of body weight. (One teaspoonful = 5 cc.)

Antiminth (pyrantel pamoate) Oral Suspension may be administered without regard to ingestion of food or time of day; and purging is not necessary prior to, during, or after therapy. It may be taken with milk or fruit juices. Because of limited data on repeated doses, no recommendations can be made

How Supplied. Antiminth is available as a pleasant tasting caramel-flavored suspension which contains the equivalent of 50 mg. pyrantel base per ml., supplied in 60 cc. bottles.

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(pyrantel pamoate)

equivalent to 50 mg. pyrantel/ml.

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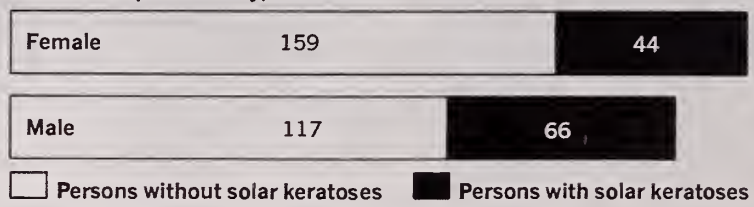
What it means to live and work in Tipton County, Tennessee

Persons who are white and over 40 have one chance in four of having solar keratoses... which may be premalignant

An epidemiologic study* conducted in Tipton County, Tennessee, revealed that 28.5% of white persons over 40 had solar keratoses; most had multiple lesions. Cluster sampling projected an estimated prevalence of 32.5% for white males and 19.5% for white females.

Though this is an unusually high percentage of affected persons, these lesions can occur in any white population, wherever people work or play out of doors.

Prevalence of solar keratoses in white persons over 40 in Tipton County, Tennessee



*Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey.



Solar, actinic, senile keratoses

Called by many names, the typical lesion is flat or slightly elevated, brownish or reddish in color, papular, dry, adherent, rough, sharply defined; usually multiple lesions, chiefly on exposed portions of the skin.

Sequence/selectivity of response

Erythema in areas of lesions may begin after several days of therapy; height of reaction (only in affected areas)* usually occurs within two weeks, declining after discontinuation of therapy. Since this response is so predictable, lesions that do not respond should be biopsied to rule out the presence of a frank neoplasm.

Cosmetic results

Cosmetic results are highly favorable. Incidence of scarring is low—important with multiple facial lesions. Efudex should be applied with care near the eyes, nose and mouth.

5% cream–a Roche exclusive

Only Roche formulates the 5% cream... high in patient acceptability... high in clinical efficacy, especially for lesions of hands and forearms... economical.

Before prescribing, please consult complete product information, a summary of which follows:
Indications: Multiple actinic or solar keratoses.
Contraindications: Patients with known hypersensitivity to any of its components.
Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.
Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.
Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.
Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.
How Supplied: Solution, 10-ml drop dispensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.
Cream, 25-Gm tubes—containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).

an alternative to conventional therapy

Efudex®

(fluorouracil)

cream/solution

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Nutley, N.J. 07110



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1972

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May 11	Recent Advances in Cardiology
May 12	Association of House Staff Physicians—Annual Meeting

For further information write:

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Pre-Sate ®
(chlorphentermine HCl)

CAUTION: Federal law prohibits dispensing without prescription.

Indications: Pre-Sate (chlorphentermine hydrochloride) is indicated in exogenous obesity, as a short term (*i.e.*, several weeks) adjunct in a regimen of weight reduction based upon caloric restriction.

Contraindications: Glaucoma, hyperthyroidism, pheochromocytoma, hypersensitivity to sympathomimetic amines, and agitated states. Pre-Sate (chlorphentermine hydrochloride) is also contraindicated in patients with a history of drug abuse or symptomatic cardiovascular disease of the following types: advanced arteriosclerosis, severe coronary artery disease, moderate to severe hypertension, or cardiac conduction abnormalities with danger of arrhythmias. The drug is also contraindicated during or within 14 days following administration of monamine oxidase inhibitors, since hypertensive crises may result.

Warnings: When weight loss is unsatisfactory the recommended dosage should not be increased in an attempt to obtain increased anorexigenic effect; discontinue the drug. Tolerance to the anorectic effect may develop. Drowsiness or stimulation may occur and may impair ability to engage in potentially hazardous activities such as operating machinery, driving a motor vehicle, or performing tasks requiring precision work or critical judgment. Therefore, such patients should be cautioned accordingly. Caution must be exercised if Pre-Sate (chlorphentermine hydrochloride) is used concomitantly with other central nervous system stimulants. There have been reports of pulmonary hypertension in patients who received related drugs.

Drug Dependence: Drugs of this type have a potential for abuse. Patients have been known to increase the intake of drugs of this type to many times the dosages recommended. In long-term controlled studies with high dosages of Pre-Sate, abrupt cessation did not result in symptoms of withdrawal.

Usage In Pregnancy: The safety of Pre-Sate (chlorphentermine hydrochloride) in human pregnancy has not yet been clearly established. The use of anorectic agents by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and child. Use of the drug during lactation is not recommended. Mammalian reproductive and teratogenic studies with high multiples of the human dose have been negative.

Usage In Children: Not recommended for use in children under 12 years of age.

Precautions: In patients with diabetes mellitus there may be alteration of insulin requirements due to dietary restrictions and weight loss. Pre-Sate (chlorphentermine hydrochloride) should be used with caution when obesity complicates the management of patients with mild to moderate cardiovascular disease or diabetes mellitus, and only when dietary restriction alone has been unsuccessful in achieving desired weight reduction. In prescribing this drug for obese patients in whom it is undesirable to introduce CNS stimulation or pressor effect, the physician should be alert to the individual who may be overly sensitive to this drug. Psychologic disturbances have been reported in patients who concomitantly receive an anorexic agent and a restrictive dietary regimen.

Adverse Reactions: Central Nervous System: When CNS side effects occur, they are most often manifested as drowsiness or sedation or overstimulation and restlessness. Insomnia, dizziness, headache, euphoria, dysphoria, and tremor may also occur. Psychotic episodes, although rare, have been noted even at recommended doses. **Cardiovascular:** tachycardia, palpitation, elevation of blood pressure. **Gastrointestinal:** nausea and vomiting, diarrhea, unpleasant taste, constipation. **Endocrine:** changes in libido, impotence. **Autonomic:** dryness of mouth, sweating, mydriasis. **Allergic:** urticaria. **Genitourinary:** diuresis and, rarely, difficulty in initiating micturition. **Others:** Paresthesias, sural spasms.

Dosage and Administration: The recommended adult daily dose of Pre-Sate (chlorphentermine hydrochloride) is one tablet (equivalent to 65 mg chlorphentermine base) taken after the first meal of the day. Use in children under 12 not recommended.

Overdosage: Manifestations: Restlessness, confusion, assaultiveness, hallucinations, panic states, and hyperpyrexia may be manifestations of acute intoxication with anorectic agents. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension, or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.

Management: Management of acute intoxication with sympathomimetic amines is largely symptomatic and supportive and often includes sedation with a barbiturate. If hypertension is marked, the use of a nitrate or rapidly acting alpha-receptor blocking agent should be considered. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard.

How Supplied: Each Pre-Sate (chlorphentermine hydrochloride) tablet contains the equivalent of 65 mg chlorphentermine base; bottles of 100 and 1000 tablets.

Full information available on request.

WARNER-CHILCOTT
Division, Warner-Lambert Company
Morris Plains, New Jersey 07950



Pre-Sate® (chlorphentermine HCl)...the increasingly practical appetite suppressant



When you select this familiar antibiotic for IV infusion you have available a broad dosage range that hospitalized patients may need.

Intravenous Lincocin (lincomycin hydrochloride, Upjohn), with its 1.2 to 8 grams/day dosage range, covers many serious and even life-threatening infections. Lincocin is effective in infections due to susceptible strains of streptococci, pneumococci, and staphylococci. Lincocin IV therefore can be as useful in your hospitalized patients as its IM use has proved to be in your office patients. As with all antibiotics, *in vitro* susceptibility studies should be performed.

1.2 to 8 grams/day IV dosage range: Most hospitalized patients with uncomplicated pneumonias respond satisfactorily to 1.2 to 1.8 grams/day of Lincocin IV. These doses may have to be increased for more serious infections. In life-threatening situations as much as 8 grams/day has been administered intravenously to adults.

In usual IV doses, Lincocin (lincomycin hydrochloride, Upjohn) should be diluted in 250 ml or more of normal saline solution or 5% glucose in water. But when 4 grams or more per day is given, Lincocin should be diluted in not less than 500 ml of either solution, and the rate of administration should not exceed 100 ml/hour. Too rapid intravenous administration of doses exceeding 4 grams may result in hypotension or, in rare instances, cardiopulmonary arrest.

Effective gram-positive antibiotic: Lincocin IV is effective in respiratory tract, skin and soft-tissue, and bone

infections caused by susceptible strains of pneumococci, streptococci, and staphylococci, including penicillin-resistant strains. Staphylococcal strains resistant to Lincocin (lincomycin hydrochloride, Upjohn) have been recovered. Before initiating therapy, culture and susceptibility studies should be performed. Lincocin has proved valuable in treating patients hypersensitive to penicillin or cephalosporins, since Lincocin does not share antigenicity with these compounds. However, hypersensitivity reactions have been reported, some of these in patients known to be sensitive to penicillin.

Well tolerated at infusion site: Lincocin intravenous infusions have not produced local irritation or phlebitis, when given as recommended. Lincocin is usually well tolerated in patients who are hypersensitive to other drugs. Nevertheless, Lincocin should be used cautiously in patients with asthma or significant allergies.

In patients with impaired renal function, the recommended dose of Lincocin should be reduced to 25–30% of the dose for patients with normal kidney function. Its safety in pregnant patients and in infants less than one month of age has not been established.

Lincocin may be used with other antimicrobial agents: Since Lincocin is stable over a wide pH range, it is suitable for incorporation in intravenous infusions; it also may be administered concomitantly with other antimicrobial agents when indicated. However, Lincocin should not be used with erythromycin, as *in vitro* antagonism has been reported.

Lincocin®

Sterile Solution (300 mg per ml)

(lincomycin hydrochloride, Upjohn)

For further prescribing information, please see following page.



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Sterile Solution (300 mg. per ml.)

Lincocin®

(lincomycin hydrochloride, Upjohn)

Up to 8 grams per day by IV infusion for hospitalized patients with life-threatening infections. Lincocin is effective in infections due to susceptible strains of streptococci, pneumococci, and staphylococci. As with all antibiotics, *in vitro* susceptibility studies should be performed.

Each preparation contains:	Lincomycin hydrochloride monohydrate equivalent to lincomycin base
250 mg Pediatric Capsule	250 mg
500 mg Capsule	500 mg
*Sterile Solution per 1 ml	300 mg
Syrup per 5 ml	250 mg

*Contains also: Benzyl Alcohol 9 mg; and, Water for Injection—q.s.

Lincocin (lincomycin hydrochloride) is indicated in infections due to susceptible strains of staphylococci, pneumococci, and streptococci. *In vitro* susceptibility studies should be performed. Cross resistance has not been demonstrated with penicillin, ampicillin, cephalosporins, chloramphenicol or the tetracyclines. Some cross resistance with erythromycin has been reported. Studies indicate that Lincocin does not share antigenicity with penicillin compounds.

CONTRAINDICATIONS: History of prior hypersensitivity to lincomycin or clindamycin. Not indicated in the treatment of viral or minor bacterial infections.

WARNINGS: *CASES OF SEVERE AND PERSISTENT DIARRHEA HAVE BEEN REPORTED AND HAVE AT TIMES NECESSITATED DISCONTINUANCE OF THE DRUG. THIS DIARRHEA HAS BEEN OCCASIONALLY ASSOCIATED WITH BLOOD AND MUCUS IN THE STOOLS AND HAS AT TIMES RESULTED IN AN ACUTE COLITIS. THIS SIDE EFFECT USUALLY HAS BEEN ASSOCIATED WITH THE ORAL DOSAGE FORM BUT OCCASIONALLY HAS BEEN REPORTED FOLLOWING PARENTERAL THERAPY.* A careful inquiry should be made concerning previous sensitivities to drugs or other allergens. Safety for use in pregnancy has not been established and Lincocin (lincomycin hydrochloride) is not indicated in the newborn. Reduce dose 25 to 30% in patients with severe impairment of renal function.

PRECAUTIONS: Like any drug, Lincocin should be used with caution in patients having a history of asthma or significant allergies. Overgrowth of nonsusceptible organisms, particularly yeasts, may occur and require appropriate measures. Patients with pre-existing monilial infections requiring Lincocin therapy should be given concomitant antimonilial treatment. During prolonged Lincocin therapy, periodic liver function studies and blood counts should be performed. Not recommended (inadequate data) in patients with pre-existing liver disease unless special clinical circumstances indicate. Continue treatment of β-hemolytic streptococci infections for 10 days to diminish likelihood of rheumatic fever or glomerulonephritis.

ADVERSE REACTIONS: *Gastrointestinal*—Glossitis, stomatitis, nausea, vomiting. Persistent diarrhea, enterocolitis, and pruritus ani. *Hemopoietic*—Neutropenia, leukopenia, agranulocytosis, and thrombocytopenic purpura have been reported. *Hypersensitivity reactions*—Hypersensitivity reactions such as angioneurotic edema, serum sickness, and anaphylaxis have been reported, sometimes in patients sensitive to penicillin. If allergic reaction occurs, discontinue drug. Have epinephrine, corticosteroids, and antihistamines available for emergency treatment. *Skin and mucous membranes*—Skin rashes, urticaria, vaginitis, and rare instances of exfoliative and vesiculobullous dermatitis have been reported. *Liver*—Although no direct relationship to liver dysfunction is established, jaundice and abnormal liver function tests (particularly serum transaminase) have been observed in a few instances. *Cardiovascular*—Instances of hypotension following parenteral administration have been reported, particularly after too rapid IV administration. Rare instances of cardiopulmonary arrest have been reported after too rapid IV administration. If 4.0 grams or more administered IV, dilute in 500 ml of fluid and administer no faster than 100 ml per hour. *Special senses*—Tinnitus and vertigo have been reported occasionally. *Local reactions*—Excellent local tolerance demonstrated to intramuscularly administered Lincocin (lincomycin hydrochloride). Reports of pain following injection have been infrequent. Intravenous administration of Lincocin in 250 to 500 ml of 5% glucose in distilled water or normal saline has produced no local irritation or phlebitis.

HOW SUPPLIED: *250 mg* and *500 mg* Capsules—bottles of 24 and 100. *Sterile Solution, 300 mg per ml*—2 and 10 ml vials and 2 ml syringe. *Syrup, 250 mg per 5 ml*—60 ml and pint bottles.

For additional product information, consult the package insert or see your Upjohn representative.

MED B-6-S (KZL-7) JA71-1631

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Kalamazoo, Michigan 49001

Upjohn



rheumatoid arthritic blowup...

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oxyphenbutazone NF

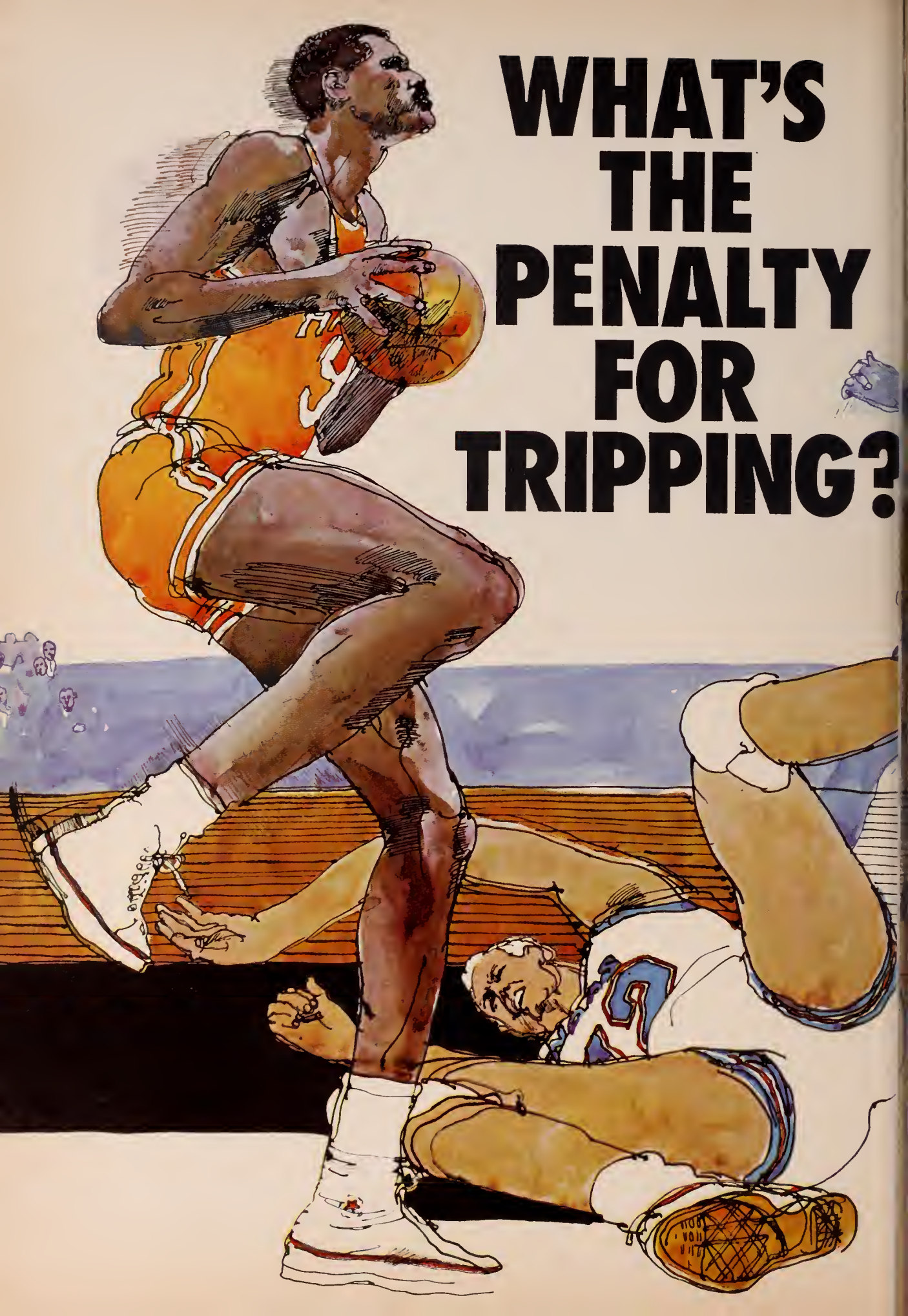
tablets of 100 mg.

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral lesions (symptoms of blood dyscrasia); dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.
Indications: Acute gouty arthritis, rheumatoid arthritis, rheumatoid spondylitis.
Contraindications: Children 14 years or less; senile patients; history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypertension; thyroid disease; systemic edema; stomatitis and salivary gland enlargement due to the drug; polymyalgia rheumatica and temporal arteritis; patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.
Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpredictable benefits against potential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.
Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.
Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angiitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement.
(B) 98-146-800-E

For complete details, including dosage, please see full prescribing information.

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardsley, New York 10502

TA. 8356 .9


WHAT'S
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A personal foul against the tripper, and possibly weeks of painful skeletal muscle spasm for the victim.

For the skeletal muscle spasm of leg strains, Valium® (diazepam) can be a valuable adjunct. A dose of 2-10 mg, three or four times a day, goes to work to help break up the cycle of spasm/pain/spasm. The resultant relief of skeletal muscle spasm may permit greater mobilization of the affected muscles and may help the patient resume usual activities sooner than otherwise possible.



Sudden trauma to and unusual stress on sartorius muscle may cause strain of muscle and tearing of some of the fibers. The resultant muscle spasm can make leg motion painful.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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Nutley, N.J. 07110

VALIUM® (diazepam)

adjunct in skeletal muscle spasm

2-mg, 5-mg, 10-mg tablets

To get the water out in edema*

To lower blood pressure in hypertension*

To spare potassium in both

There's

Trademark

Dyazide®

Each capsule contains 50 mg. of Dyrenium® (brand of triamterene) and 25 mg. of hydrochlorothiazide.

Before prescribing, see complete prescribing information in SK&F literature or *PDR*.

***Indications:** Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome, late pregnancy; also steroid-induced and idiopathic edema, and edema resistant to other diuretic therapy. 'Dyazide' is also indicated in the treatment of mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, **check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., certain elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—they can both cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

Supplied: Bottles of 100 capsules.

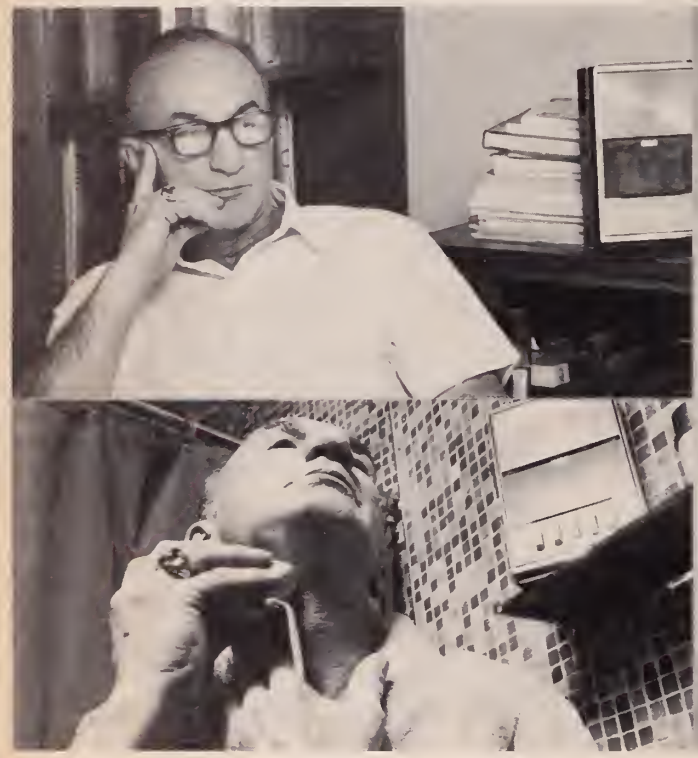
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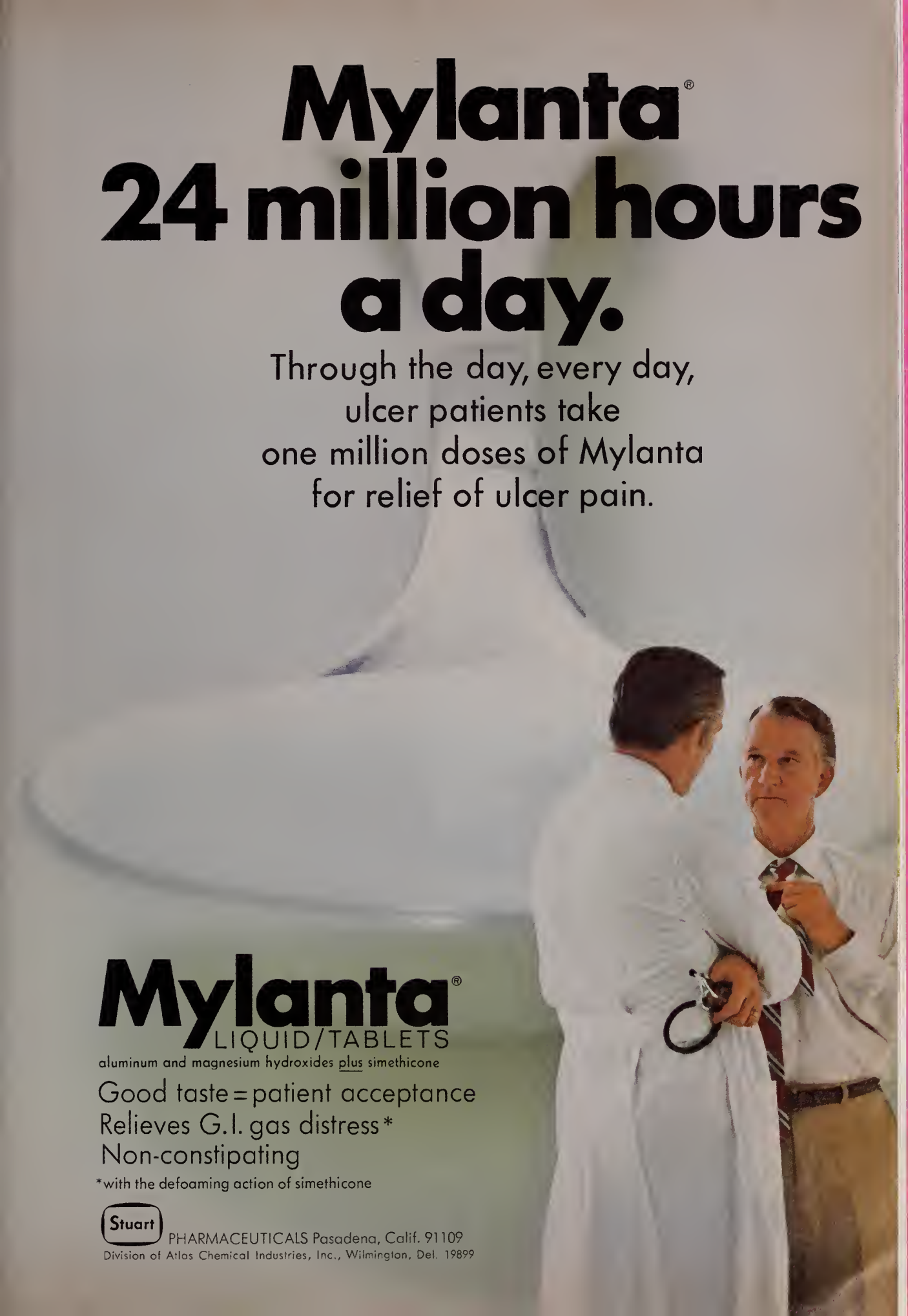
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of moderate to severe intensity

Though Talwin® can be compared to codeine in analgesic efficacy, it is not a narcotic. So patients receiving Talwin for prolonged periods face fewer of the consequences you've come to expect with narcotic analgesics. And that, in the long run, can mean a better outlook for your chronic-pain patient.

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- **Tolerance not a problem:** tolerance to the analgesic effect of Talwin Tablets has not been reported, and no significant changes in clinical laboratory parameters attributable to the drug have been reported.
- **Dependence rarely a problem:** during three years of wide clinical use, only a few cases of dependence have been reported. In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in dose by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain.
- **Not subject to narcotic controls:** convenient to prescribe—day or night—even by phone.
- **Generally well tolerated by most patients:** infrequently cause decrease in blood pressure or tachycardia; rarely cause respiratory depression or urinary retention; seldom cause diarrhea or constipation. If dizziness, lightheadedness, nausea or vomiting are encountered, these effects tend to be self-limiting and to decrease after the first few doses. (See last page of this advertisement for a complete discussion of adverse reactions and a brief discussion of other Prescribing Information.)

50 mg. Tablets

Talwin®

brand of

pentazocine (as hydrochloride)

the long-range analgesic

a new outlook in chronic pain

of moderate to severe intensity



Contraindications: Talwin, brand of pentazocine (as hydrochloride), should not be administered to patients who are hypersensitive to it.

Warnings: *Head Injury and Increased Intracranial Pressure.* The respiratory depressant effects of Talwin and its potential for elevating cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a preexisting increase in intracranial pressure. Furthermore, Talwin can produce effects which may obscure the clinical course of patients with head injuries. In such patients, Talwin must be used with extreme caution and only if its use is deemed essential.

Usage in Pregnancy. Safe use of Talwin during pregnancy (other than labor) has not been established. Animal reproduction studies have not demonstrated teratogenic or embryotoxic effects. However, Talwin should be administered to pregnant patients (other than labor) only when, in the judgment of the physician, the potential benefits outweigh the possible hazards. Patients receiving Talwin during labor have experienced no adverse effects other than those that occur with commonly used analgesics. Talwin should be used with caution in women delivering premature infants.

Drug Dependence. There have been instances of psychological and physical dependence on parenteral Talwin in patients with a history of drug abuse and, rarely, in patients without such a history. Abrupt discontinuance following the extended use of parenteral Talwin has resulted in withdrawal symptoms. There have been a few reports of dependence and of withdrawal symptoms with orally administered Talwin. Patients with a history of drug dependence should be under close supervision while receiving Talwin orally.

In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in dose by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain.

Acute CNS Manifestations. Patients receiving therapeutic doses of Talwin have experienced, in rare instances, hallucinations (usually visual), disorientation, and confusion which have cleared spontaneously within a period of hours. The mechanism of this reaction is not known. Such patients should be very closely observed and vital signs checked. If the drug is reinstituted it should be done with caution since the acute CNS manifestations may recur.

Usage in Children. Because clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Ambulatory Patients. Since sedation, dizziness, and occasional euphoria have been noted, ambulatory patients should be warned not to operate machinery, drive cars, or unnecessarily expose themselves to hazards.

Precautions: *Certain Respiratory Conditions.* Although respiratory depression has rarely been reported after oral administration of Talwin, the drug should be administered with caution to patients with respiratory depression from any cause, severe bronchial asthma and other obstructive respiratory conditions, or cyanosis.

Impaired Renal or Hepatic Function. Decreased metabolism of the drug by the liver in extensive liver disease may predispose to accentuation of side effects. Although laboratory tests have not indicated that Talwin causes or increases renal or hepatic impairment, the drug should be administered with caution to patients with such impairment.

Myocardial Infarction. As with all drugs, Talwin should be used with caution in patients with myocardial infarction who have nausea or vomiting.

Biliary Surgery. Until further experience is gained with the effects of Talwin on the sphincter of Oddi, the drug should be used with caution in patients about to undergo surgery of the biliary tract.

Patients Receiving Narcotics. Talwin is a mild narcotic antagonist. Some patients previously receiving narcotics have experienced mild withdrawal symptoms after receiving Talwin.

CNS Effect. Caution should be used when Talwin is administered to patients prone to seizures; seizures have occurred in a few such patients in association with the use of Talwin although no cause and effect relationship has been established.

Adverse Reactions: Reactions reported after oral administration of Talwin include *gastrointestinal:* nausea, vomiting; infrequently constipation; and rarely abdominal distress, anorexia, diarrhea. *CNS effects:* dizziness, lightheadedness, sedation, euphoria, headache; infrequently weakness, disturbed dreams, insomnia, syncope, visual blurring and focusing difficulty, hallucinations (see *Acute CNS Manifestations* under WARNINGS); and rarely tremor, irritability, excitement, tinnitus. *Autonomic:* sweating; infrequently flushing; and rarely chills. *Allergic:* infrequently rash; and rarely urticaria, edema of the face. *Cardiovascular:* infrequently decrease in blood pressure, tachycardia. *Other:* rarely respiratory depression, urinary retention.

Dosage and Administration: *Adults.* The usual initial adult dose is 1 tablet (50 mg.) every three or four hours. This may be increased to 2 tablets (100 mg.) when needed. Total daily dosage should not exceed 600 mg.

When antiinflammatory or antipyretic effects are desired in addition to analgesia, aspirin can be administered concomitantly with Talwin.

Children Under 12 Years of Age. Since clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Duration of Therapy. Patients with chronic pain who have received Talwin orally for prolonged periods have not experienced withdrawal symptoms even when administration was abruptly discontinued (see WARNINGS). No tolerance to the analgesic effect has been observed. Laboratory tests of blood and urine and of liver and kidney function have revealed no significant abnormalities after prolonged administration of Talwin.

Overdosage: *Manifestations.* Clinical experience with Talwin overdosage has been insufficient to define the signs of this condition.

Treatment. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated. Assisted or controlled ventilation should also be considered. Although nalorphine and levallorphan are *not* effective antidotes for respiratory depression due to overdosage or unusual sensitivity to Talwin, parenteral naloxone (Narcan®, available through Endo Laboratories) is a specific and effective antagonist. If naloxone is not available, parenteral administration of the analeptic, methylphenidate (Ritalin®), may be of value if respiratory depression occurs.

Talwin is not subject to narcotic controls.

How Supplied: Tablets, peach color, scored. Each tablet contains Talwin (brand of pentazocine) as hydrochloride equivalent to 50 mg. base. Bottles of 100.

Winthrop Winthrop Laboratories, New York, N. Y. 10016 (1583)

50 mg. Tablets

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pentazocine (as hydrochloride)

the long-range analgesic

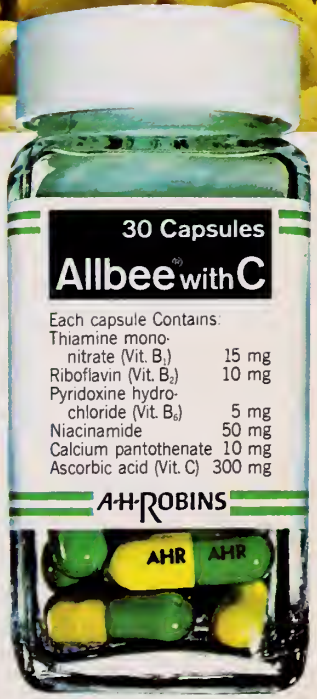


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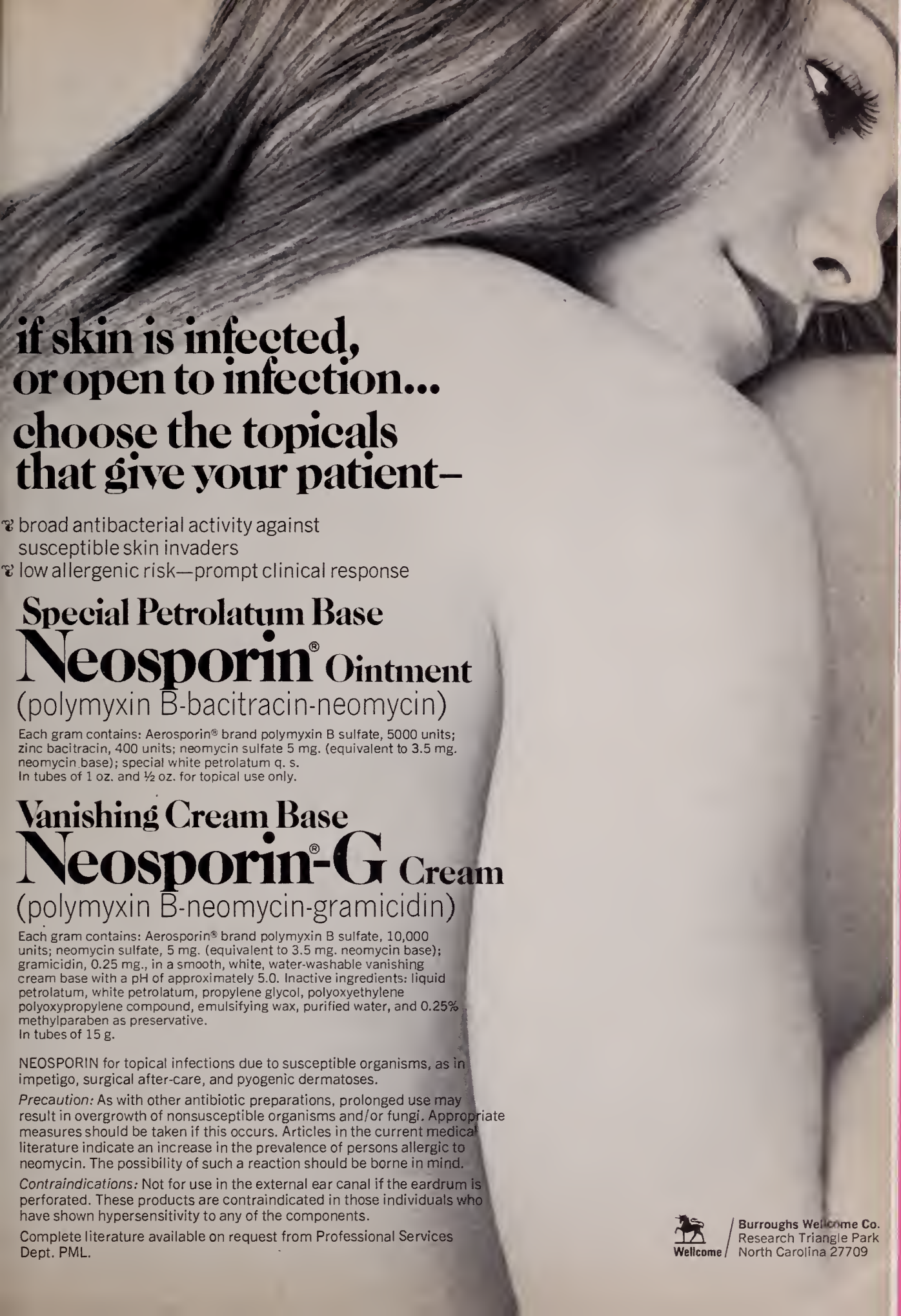
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hyoscyamine sulfate	0.1037 mg.	0.1037 mg.	0.3111 mg.
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hyoscine hydrobromide	0.0065 mg.	0.0065 mg.	0.0195 mg.
phenobarbital (warning: may be habit forming)	(¼ gr.) 16.2 mg.	(½ gr.) 32.4 mg.	(¾ gr.) 48.6 mg.

Brief summary. Side effects: Blurring of vision, dry mouth, difficult urination, and flushing or dryness of the skin may occur on higher dosage levels, rarely on usual dosage. Administer with caution to patients with incipient glaucoma or urinary bladder neck obstruction as in prostatic hypertrophy. Contraindicated in patients with acute glaucoma, advanced renal or hepatic disease or hypersensitivity to any of the ingredients.

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NEOSPORIN for topical infections due to susceptible organisms, as in impetigo, surgical after-care, and pyogenic dermatoses.

Precaution: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Contraindications: Not for use in the external ear canal if the eardrum is perforated. These products are contraindicated in those individuals who have shown hypersensitivity to any of the components.

Complete literature available on request from Professional Services Dept. PML.

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Contraindications: Hypersensitivity to barbiturates or belladonna alkaloids, glaucoma, advanced renal or hepatic disease.
Precautions: Administer with caution to patients with incipient glaucoma, bladder neck obstruction or urinary bladder atony. Prolonged use of barbiturates may be habit-forming.
Side effects: Blurred vision, dry mouth, dysuria, and other atropine-like side effects may occur at high doses, but are only rarely noted at recommended dosages.
Dosage: Adults: One or two tablets three or four times daily. Dosage can be adjusted depending on diagnosis and severity of symptoms. Children 2 to 12 years: One half or one tablet three or four times daily. Tablets may be chewed or swallowed with liquids.

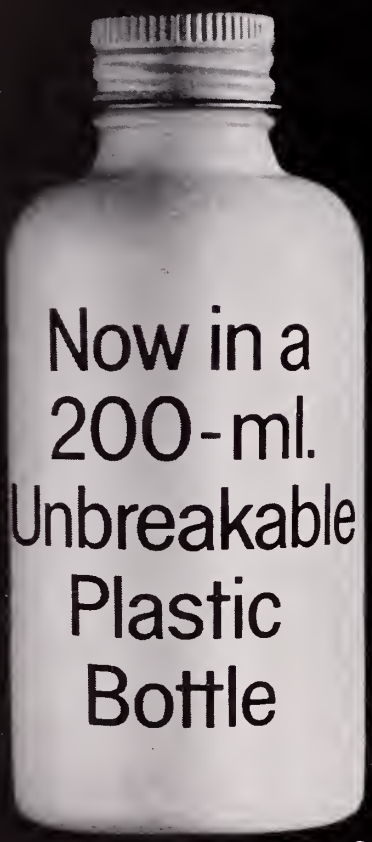
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to move,
and the Latin **sedatus,**
to calm)

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Old Fashioned Refreshment

ONE OF THE oldest truths in clinical medicine is that no two cases of an illness are exactly alike. The variations of a given disease are as infinite as the number of victims it can attack. The least experienced physician understands this and is not often deceived by the masquerades of a common illness.

As no two cases of an illness are identical, no two treatment programs can be identical. Indeed, as the treatment of a sick human being involves his biologic, psychologic, sociologic, economic and familial relationships and needs, the variations inherent in the treatment of two patients with the same disease are also infinite.

As a simplified example consider the problems of two middle aged women who are stricken with pneumonia: One is stoic and has great confidence in her physician's skill and knowledge, while the other is frightened, a stranger to her physician and allergic to penicillin, tetracycline and sulfa drugs. The husband of the stoic patient is calm, resourceful and attentive to his wife's needs; they have one daughter who is married and lives in a distant city. The husband of the frightened patient is boorish, tyrannical, thoroughly egocentric and suspicious of most physicians and all strangers; they have one son and four daughters, all of whom share the personality traits of both parents.

Given these few but not uncommon variations in two "cases of pneumonia," the most callow clinician can anticipate the great dissimilarity which will develop between the programs of treatment essential to recovery in both cases.

To deny these obvious truths . . . to ignore these patent facts is to embrace moronism. When we physicians allow our services to be priced and tagged as items of merchandise, we become party to that moronism. As such, we deserve to be treated as price-haggling peddlers.

We are professional servants, engaged in the delivery of personal services. A wide variety of these services are requested by a wider variety of individuals with an even wider variety of needs. Because of these variations, no price tag can apply to all cases which are similar in name. Our fees must reflect the kinds and amounts of services we render; the time we spend in all aspects of case management; the nature and extent of our training and experience; the liability we assume and the responsibility we bear. Also, our fees and how they are collected should reflect a concern for our patients' economic welfare and his sense of dignity.

If we insisted that these principles serve as the *only* "guideline" for our fees, we would not find ourselves standing at the curb, accused of "overcharging" our merchandise. We would realize again, after all these years, that we are not engaged in mercantilism.

How old fashioned!

How refreshing!—*MRJ* □



The evolution of the family practice physician from that of the compassionate comforter of early American medicine has been aided and abetted by sociological, economic, scientific and political factors over which he has exercised little or no control. The population explosion, the increased standard of living and more widespread affluence, astounding advances in medicine including phenomenal technological progress and better transportation among others have been most important.

Concomitantly there have developed problems in education, ecology, poverty, ignorance and racism. Medicine has been caught in the mainstream of these changes and as a result has undergone a transition from generalism to specialism with the result that the family doctor concept is in danger of going down the drain and being replaced by the concept of the primary physician.

There are an estimated 51,000 general practice physicians, inclusive of 3,285 newly certified specialists in family practice. They are still in great demand since the needs of the expanding population remain the same and the majority of their complaints are responsive to this group.

The family practice type of physician has been the foundation upon which American medicine has been built and it may be our last hope in preserving the practice of medicine in the United States as a free enterprise. He is in the best position for maintaining the kind of physician-patient relationship without which our present type of practice cannot exist. This does not mean to imply that specialists cannot contribute to an environment of public trust between doctor and patient. However, the opportunity for practice of personalized medicine which we hope our patients will continue to seek is much greater in the sphere of family practice.

I see this trend toward the training of more family practice specialists as a necessity for the preservation of this public trust. Let all of us as physicians encourage and assist this trend; at the same time keeping in mind that a combination of general practitioner, specialist and sub-specialist guarantee good quality and progressive medical care.

The past year has been interesting and exciting for me; rewarding also in many aspects not financial. It has not lacked accomplishments, due mainly to the unstinting cooperation of the headquarters staff of Blair, Bickham and Kelsay. Serious problems still confront us, which will be assumed by Dr. Stanley McCampbell, who, I can say with assurance, is most energetic and extremely capable.

Sincerely,

Lucien E. Pascuzzi

OSMA JOURNAL/scientific

Modification of Drug Dosages in Renal Disease

THOMAS L. WHITSETT, MD

The plasma level and toxic effects of certain drugs are altered by renal disease. Failure to take this into account may compound the existing illness.

BLOOD LEVELS achieved with standard doses of pharmacological agents are frequently quite variable among patients with normal renal function. However, these variations in bio-availability are relatively minor compared to the magnitude of the problem which may be encountered in individuals with impaired renal function. Two recent reviews of this subject[1, 2] have gone into considerable detail on the matter and are recommended for a more exhaustive analysis of the problem. The present paper briefly summarizes renal mechanisms of drug disposition and presents the major factors referable to selecting appropriate drugs in proper dosages in patients with renal disease. The tables were modified from the review by Bennett, *et al.*[2]

This is a continuation of the papers presented during the symposium on "New Challenges in Renal Disease" March 17th, 1971, which was sponsored by the Kidney Foundation of Oklahoma-Southern Kansas, Inc., the Association of the University of Oklahoma Medical Faculty and the Oklahoma Regional Medical Program.

GENERAL PRINCIPLES

The major avenues of eliminating pharmacologic agents from the body are drug metabolism and the renal excretion of either the parent compound or its metabolites. The disposition of certain drugs is handled predominantly by one of these two mechanisms, while other agents are dependent on both mechanisms. However, in certain instances, one of these factors is depressed, *e.g.*, impaired renal function, the other is capable of accelerating its activity in an attempt to achieve a somewhat constant rate of elimination.

There are basically three factors involved in the renal excretion of drugs. 1) Glomerular filtration. Only free drug (non-protein bound) is available for filtration; 2) Tubular reabsorption. Drugs which are lipid soluble and in a non-ionized state are readily reabsorbed. Thus, ionization in the glomerular filtrate of an acidic drug, *e.g.*, phenobarbital and acetyl salicylic acid, is facilitated by alkalinization of the urine resulting in decreased reabsorption and increased excretion; and 3) Renal secretion. Renal tubular secretion involves active transport and is unrelated to protein binding.

The net effect of these three factors results in the removal of a fairly constant fraction of the drug presented to the kidney by arterial blood. Thus it is clear that if the

major route of drug elimination is by one or more of these mechanisms, impaired renal function will prolong the half-life, *i.e.*, the time required for one-half of a given drug to be removed from the blood. However, if hepatic metabolism is capable of assuming the dominant role of drug elimination, then renal function is of only minor importance.

The major objective in regulating drug dosage is to achieve a reasonably constant blood level. Thus, in a patient with impaired renal function of a degree which interferes with drug elimination, the initial or loading dose should remain unchanged since an adequate blood level is necessary to produce the desired effect. However, maintenance therapy must be reduced because of the anticipated prolongation in half-life. Reduction in maintenance dosage may be accomplished by either of the following: 1) Reducing the quantity of drug administered at the usual intervals or 2) administering the usual maintenance dose less frequently. The latter is the mechanism most commonly employed and easily performed.

SPECIFIC CATEGORIES OF DRUGS

The following discussion will deal primarily with factors other than specific dosages. For information regarding the latter, the reader is directed to tables I and II or references 1 and 2.

Tables I and II present the maintenance dose intervals for patients with normal renal function and patients with varying degrees of renal failure. The classifications are based on creatinine clearance (cc/min) as follows: Mild = 50-80, Moderate = 10-50 and Severe = < 10.

Cardiovascular.

Digoxin: All but 15 percent of a given dose of digoxin is excreted, unchanged in the urine. Its rate of clearance is, for all practical purposes, equal to that of creatinine. Thus, while the so-called digitalizing dose should remain unchanged, it is of importance to adjust the maintenance dose relative to creatinine clearance. I have devised the following equation from previously reported data comparing the effect of creatinine clearance on the percent of the loading dose recommended for maintenance therapy.[3] The average maintenance dose (mg) equals $0.15 + 0.002 \times$ creatinine clearance. Thus, if creatinine clearance is 50 ml/min, the average maintenance dose would be $0.15 + (0.002 \times 50)$ or 0.25 mg/day. It should be remembered that serum potassium protects against digitalis toxicity; therefore a sudden reduction in serum potassium, *e.g.*, that seen with dialysis or the use of ion exchange resins, may precipitate digitalis intoxication.

Digitoxin should probably not be used in this setting since it normally has a longer half-life and its ultimate disposition is even more complicated.

Table I

CARDIOVASCULAR, ANTIHYPERTENSIVE AND DIURETIC AGENTS

Drug	Maintenance Dose Intervals			
		Renal Failure		
	Normal	Mild	Moderate	Severe
Cardiac Glycosides				
(a) Digoxin	q12h	q24h	q24-36h	q36-48h
(b) Digitoxin	q24h	q24h	q24-36h	q36-72h
Antihypertensives				
(a) Methyldopa	q6h	q6h	q8-12h	q12-18h
(b) Guanethidine	q24h	Unchanged	Unchanged	Unchanged
(c) Hydralazine	q8h	Unchanged	Unchanged	Unchanged
(d) Reserpine	q24h	Unchanged	Unchanged	Unchanged
Diuretics				
(a) Furosemide	q6h	Unchanged	Unchanged	Unchanged
(b) Ethacrynic Acid	q6h	q6h	q6h	Avoid
(c) Thiazides	q12h	q12h	q12h	Avoid
(d) Mercurials	q24h	q24h	Avoid	Avoid
(e) Spironolactone	q6h	q6h	Avoid	Avoid
(f) Triamterene	q12h	q12h	Avoid	Avoid

Table II
ANTIMICROBIAL AGENTS

Drug	Maintenance Dose Intervals Renal Failure			
	Normal	Mild	Moderate	Severe
Amphotericin B	q24h	q24h	q24h	q24-36h
Cephaloridine	q6h	q6h	q12h	q24-36h
Cephalothin	q6h	q6h	q6h	q8-12h
Chloramphenicol	q6h	Unchanged	Unchanged	Unchanged
Colistin	q12h	q24h	q36-60h	q60-90h
Erythromycin	q6h	Unchanged	Unchanged	Unchanged
Gentamicin	q8h	q8-12h	q12-24h	q48h
Isoniazide	q8h	q8h	q12h	q12-24h
Kanamycin	q8h	q24h	q24-72h	q72-96h
Lincomycin	q6h	q6h	q6h	q8-12h
Nitrofurantoin	q8h	q8h	Avoid	Avoid
Penicillins				
(a) Ampicillin	q6h	q6h	q6h	q8-12h
(b) Carbenicillin	q6h	q6h	q6h	q8-12h
(c) Methacillin	q4h	q4h	q4h	q8-12h
(d) Oxacillin	q6h	Unchanged	Unchanged	Unchanged
(e) Penicillin G	q8h	q8h	q8h	q12h
Streptomycin	q12h	q24h	q24-72h	q72-96h
Sulfasoxisole	q6h	q6h	q8-12h	q12-24h
Tetracycline	q6h	q12h	q24-48h	q72h
Chlortetracycline	q6h	Unchanged	Unchanged	Unchanged

Antihypertensive Agents

Guanethidine, hydralazine and reserpine are inactivated by drug metabolism; therefore in renal disease they may be prescribed in usual dosages. Of these agents, perhaps hydralazine would be the drug of choice since it does not appear to decrease glomerular filtration rate as is frequently seen with guanethidine and reserpine. There is controversy regarding the effect of methyldopa on renal blood flow. Although it probably does not increase renal blood flow, there is perhaps less depression as is seen with the agents cited above. Methyldopa is eliminated by both renal and hepatic mechanisms; consequently a moderate reduction in dose is indicated. However, dosage of an antihypertensive agent is generally titrated against blood pressure and adjusted accordingly.

Diuretic Agents

Furosemide and ethacrynic acid are potent diuretics which may be effective in individuals whose creatinine clearance is less than 30 ml/min. Furosemide is preferable to ethacrynic acid since it may be prescribed in a normal dose and has less risk relative to auditory nerve damage. Thiazides are ineffective when the creatinine clearance is less than 30 ml/min and like ethacrynic acid requires a mild restriction of dose. Mercurials, spironolactone and triameterene should be avoided in renal failure because of increased incidence of adverse effects. Caution is indicated in the over zealous use of diuretics since patients with renal disease are very sensitive to volume depletion which may result in a further decrease in glomerular filtration rate and increase in azotemia.

Antimicrobial Agents

Since the end point resulting from an adequate plasma level of an antibiotic is not as precise as it is with other forms of therapy, and measurements of plasma levels are not readily available, it is essential to know which agents are used in a normal dose and those which require varying degrees of restriction. Most of the commonly used antibiotics are listed in Table II along with the appropriate dosages.

The following antibiotics may be used in standard dosage: cephalothin, chloramphenicol, chlortetracycline, cloxacillin, erythromycin, oxacillin and novobicin. The urinary recovery of chloramphenicol is markedly reduced in renal failure making it an ineffective agent in treating bacteriuria in this setting. Also, in individuals with renal insuf-

ficiency, the tetracyclines exert an antianabolic effect which produces an increase in blood urea nitrogen and hyperphosphatemia and contributes to the metabolic acidosis.

The following antibiotics may be administered in a normal loading dose with a modest reduction of the maintenance therapy depending on the degree of renal failure: Penicillin G, ampicillin, methacillin, carbenicillin, cephaloridine and isoniazid. It is important to remember that potassium penicillin contains 1.7 mEq of potassium per one million units, and that cephaloridine may exert a direct nephrotoxic effect.

The following antibiotics require a normal loading dose and major reduction in maintenance therapy: Amphotericin B, colistin, kanamycin, gentamicin, neomycin, polymyxin B, streptomycin and tetracycline. All of these antibiotics except the latter two have a direct nephrotoxic effect and should be avoided unless definitely indicated.

Analgesics

The narcotic analgesics are primarily metabolized and only small portions are excreted unchanged in the urine. Thus, they may be administered in a normal dosage. However, patients with severe renal insufficiency are frequently supersensitive to their central nervous system depressant effects. Consequently, in this setting, a reduction in dosage may be necessary. The urinary excretion of salicylates, as mentioned in the general principle section, is pH dependent. However, on the average, 60 percent is excreted unchanged. Therefore, the serum half-life is related to renal function and in patients with moderate to severe renal disease the interval between doses should be prolonged. Phenacetin and phenylbutazone should be avoided since both agents have been associated with direct nephrotoxicity. Propoxyphene (Darvon), a narcotic derivative of limited analgesic effect, is metabolized mainly by the liver; consequently it may be administered in a normal dosage.

Hypnotics and Sedatives

As with some of the potent analgesics, hypnotic agents are prone to exert an exaggerated effect in patients with severe renal insufficiency. Amobarbital, secobarbital and chloral hydrate are primarily metabolized by the liver and consequently in renal disease a standard dose does not cause plasma levels to accumulate.

Phenobarbital is primarily excreted unchanged by the kidneys. However, there is an element of metabolism by the liver which is capable of increasing its activity if urinary excretion is impaired. Therefore, a standard dose may not accumulate in patients with renal disease. Metabolism of the phenothiazines is complex and varies from patient to patient. They also possess anticholinergic activity which may lead to urinary retention in patients with renal insufficiency. Although they are not ideal for chronic administration, they may be quite efficacious in individuals with acute toxic psychosis. Diazepam (Valium) may be used without adjustment of dosage and has been reported to be fairly well tolerated. Chlordiazepoxide (Librium) has produced marked depression and lethargy and should probably be avoided or used in a restricted dosage.

Anticonvulsants

Diphenylhydantoin (Dilantin) is primarily metabolized by the liver and may be administered in a usual dosage. Trimethadione (Tridione) which is used for the treatment of petit mal epilepsy has been reported to cause nephrotic syndrome. Consequently it should be avoided if possible, but if used only a modest reduction of dosage is indicated. Primidone (Mysoline), which is metabolized to phenobarbital, should be administered with the same precaution as stated for the latter.

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Antiacids and Cathartics

Magnesium containing agents, *e.g.*, Aludrox, Gelusil, milk of magnesia, and Maalox should be avoided since their administration could lead to magnesium intoxication. Alternatives which are free of magnesium would be Amphojel, Basaljel and Creamalin. If cathartics are required, one should avoid their unrestricted usage since patients with renal disease are quite sensitive to hypovolemia and hypokalemia.

Radiographic Contrast Media

When preparatory measures are prescribed for radiographic evaluation utilizing contrast media, it is very important not to produce dehydration secondary to vigorous cathartic therapy and fluid restriction. Dehydration may well result in further deterioration of renal function. If sodium restriction is part of the patient's therapy, one should be aware of the following concentrations of sodium in various forms of contrast media: Conray 60 percent (Na = 2.5 mEq/liter), Renographin 60 percent (Na = 171 mEq/liter) and Hypaque 50 percent (Na = 793 mEq/liter).

Treatment of Diabetes

The oral hypoglycemic agents, *e.g.*, tolbutamide, chlorpropamide and phenformin, should be avoided since renal excretion is a major route of elimination and in the presence of renal disease a prolonged half-life results. Therefore, dosage is difficult to regulate, and should hypoglycemia develop, treatment would most likely be required for an extended period of time. Insulin is administered in a usual dose. However, it should be remembered that urinary glucose levels are an unreliable method of following the results of therapy in patients with renal disease.

Treatment of Gout

Elevated serum uric acid associated with renal disease is not an absolute indication for treatment. However, if primary or secondary gout exists, then a rational approach to therapy should be initiated. Colchicine may be administered in a standard dosage, but care should be taken to avoid dehydration secondary to its side effects. Allopurinol is effective but should be administered with a moderate restriction of dose. Should indomethacin be indicated no restriction of dosage is necessary. Probenecid should be avoided since in the presence of renal disease there is an increased tendency for the development of urolithiasis.

Miscellaneous

Azathioprine in the usual dosage has an increased incidence of toxicity in patients with decreased renal function. It should be mentioned that azathioprine is metabolized by the enzyme, xanthine oxidase, and if allopurinol (which inhibits this enzyme) is administered concurrently there will be an accumulation of the plasma levels of azathioprine.

Adrenal corticosteroids, which are occasionally used in the treatment of renal disease, are primarily metabolized by the liver; therefore, an alteration of dosage is not required.

In conclusion, the use of pharmacologic agents in patients with impaired renal function requires an understanding of the mechanism whereby a specific drug is inactivated and/or eliminated from the body. Certain drugs that are structurally related have opposite modes of disposition; therefore knowledge referable to specific agents is mandatory. The failure to appreciate these factors may result in hazardous intoxication. Also the reduction in maintenance dosage would result in failure to achieve the desired effect if the primary route of elimination is other than renal. □

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Drug Related Iatrogenic Renal Disease: The Antibiotics and Anesthetics

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Eight million persons are afflicted with renal disease in the United States each year. They are subject to an increased incidence of serious infections and physicians must be aware of the potential for aggravating or inciting renal insufficiency with potent nephrotoxic antibiotics and anesthetics

DISEASES OF IATROGENIC origin are being recognized with greater frequency. Between 1955 and 1967, patient complications from modern hospital care increased from 5% to 24% with adverse drug reactions producing most of the problems.[1-3]

At the present time the frequency of drug related iatrogenic renal disease is not known but renal impairment may be encountered in 25% to 80% of individuals receiving selected pharmaceutical agents.[4-5]

The broad spectrum antimicrobials and the anesthetic, methoxyflurane, are cited as agents commonly producing renal disorders. This discussion will briefly review a classification of adverse drug effects on the kidney and elaborate on the problems encountered with methoxyflurane as well as the known nephrotoxic antimicrobial compounds.

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TYPES OF ADVERSE DRUG EFFECTS ON THE KIDNEY

Schriener divides adverse renal drug effects into five overlapping groups.[6] Briefly, these are: A) DIRECT EFFECTS which engender acute, dose dependent, reproducible, selective or diffuse cytotoxic changes in renal structure and or function; B) ISCHEMIC EFFECTS indirectly cause diffuse changes in renal structure or function due to acute or subacute hypoxemia; C) HYPERSENSITIVITY EFFECTS arising from acute or subacute immune reactions initiate diffuse structural changes within the kidney unrelated to the amount of drug received; D) CHRONIC or SUBACUTE EFFECTS, due to cytoxic or mixed mechanisms, produce slowly evolving changes in renal structure or function which are usually noted during epidemiologic investigation; E) PREDISPOSING EFFECTS acting through several mechanisms, alter the cellular environment subacutely or chronically and promote de novo development of disease or enable preexisting disease to become evident.

The adverse renal responses produced by a single pharmaceutical agent may be classified under one or more of the five drug effect groups and each group may be associated with one or more forms of renal impairment. Some of the renal disorders and associated drugs in these five drug effect groups are presented in Table I.

Table 1
ADVERSE RENAL EFFECTS: SPECTRUM AND DRUGS

DIRECT EFFECTS

FANCONI SYNDROME
organic mercurials, degraded tetracycline
NEPHROGENIC DIABETES INSIPIDUS
lithium, methoxyflurane, demethylchlortetracycline
OLIGURIC TUBULAR NECROSIS
mercurials, bismuth, uranium, gold, iron, kanamycin, polymyxin B, colistin, cephaloridine, bacitracin, neomycin, amphotericin B, sulfonamides, ethionamide, phenylbutazone, acetazolamide

ISCHEMIC EFFECTS

DEFECTIVE EXCRETION OR CONCENTRATION
antihypertensive drugs
OLIGURIC TUBULAR NECROSIS
antihypertensive drugs, quinine, primaquine
CORTICAL NECROSIS
antihypertensive drugs, quinine

HYPERSENSITIVITY EFFECTS

GLOMERULITIS
sulfonamides, penicillin, methicillin, amphotericin B, organic mercurials, acetazolamide, allopurinol
NEPHROTIC SYNDROME
organic mercurials, tridione, paradione, gold, bismuth, tolbutamide, phenylbutazone, penicillamine, probenecid, amphotericin B
TUBULO-INTERSTITIAL NEPHRITIS
sulfonamides, phenindione, acetazolamide, phenylbutazone, phenacetin, methicillin
VASCULITIS
penicillin, methicillin, phenacetin, sulfonamide, amphotericin B, thiazides, phenylbutazone, iodides, quinine, phenindione, allopurinol

CHRONIC EFFECTS

TUBULO INTERSTITIAL NEPHRITIS
phenacetin, salicylates
NEPHROCALCINOSIS
vitamin D

PREDISPOSING EFFECTS

TUBULO INTERSTITITAL NEPHRITIS
phenacetin, kaluretics, mannitol, salicylates, dextran
RETROPERITONEAL FIBROSIS
methyseride
OBSTRUCTIVE UROPATHY
sulfonamides, salicylates, zoxazolamine, antacids, chemotherapeutic agents, antihistamines, vagolytic agents

ANTIMICROBIALS AND ADVERSE RENAL EFFECTS

Antimicrobial agents are among the most potent and frequently used drugs in modern medical practice. The drugs of major concern with respect to iatrogenic renal disease are those preferentially excreted and concentrated by the kidney, such as the aminoglycoside, polypeptide, tetracycline and amphotericin antibiotics. Renal dysfunction follows use of the penicillins and sulfonamides less frequently.

THE AMINOGLYCOSIDES: The aminoglycoside antibiotics in descending order of nephrotoxicity are neomycin, paromomycin, kanamycin, gentamycin, and streptomycin. Non-renal complications associated with these drugs include ototoxicity and myoneural blockade with respiratory arrest. The current preparations of streptomycin are not nephrotoxic but may produce modest proteinuria due to an irritative effect.[7]

Kanamycin, paromomycin and neomycin produce similar signs of nephrotoxicity.[7] These manifestations are decreased glomerular filtration, depressed renal blood flow, impaired urinary concentrating ability, increasing azotemia, albuminuria, cylindruria and microscopic hematuria. If administration of the drugs is continued after signs of nephrotoxicity appear, oliguric tubular necrosis, acute uremia and deafness rapidly develop.

With variable frequency, signs of nephrotoxicity occur in 15% to 75% of individuals receiving neomycin parenterally.[8] Renal injury also occurs when the drug is given orally,[9, 10] as a wound irrigant[11] or with serous cavity instillation.[12, 13] Up to 50% of the individuals receiving parenteral kanamycin may develop signs of nephrotoxicity.[10] In individuals with prior renal dysfunctions, use of either neomycin or kanamycin for preoperative bowel preparation can be hazardous for the small quantities absorbed will accumulate and potentiate further renal impairment.[14]

Gentamycin, the newest member of the aminoglycoside group, is associated with microscopic alteration of the urinary sediment and elevation of the blood urea nitrogen in less than 2% of individuals with previously normal renal function receiving recommended doses of the drug.[15] The incidence of nephropathy with larger doses or in patients with pre-existing renal disease may be greater.

THE POLYPEPTIDES: The polypeptide family of antibiotics, include bactracin, polymyxin B and colistin. Bacitracin was withdrawn as a parenteral medication because after three to four days treatment all recipients developed one or more signs of nephrotoxicity.[8] The depressed glomerular filtration, decreased renal tubular function and destructive lesions of the proximal and distal renal tubules were frequently persistent.

Polymyxin B and colistin are closely related compounds which are more nephrotoxic than kanamycin.[15] These drugs may also produce paresthesias and respiratory arrest. The signs of renal toxicity are proteinuria, azotemia, cellular casts, loss of urinary concentrating ability and occasionally hematuria. Glomerular function is well maintained until renal tubular necrosis occurs.

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Parenteral colistin, at the recommended dose, causes nephrotoxicity in 20% of the drug utilizations.[4] No comparable study for polymyxin B is available but the frequency is thought to be low at doses of less than 2.5 mg/kg in patients with normal renal function.[8]

THE TETRACYCLINES: Three problems related to renal disease are encountered with tetracycline compounds. First, because of the catabolic effect of tetracycline, an inordinate rise in the level of the blood urea nitrogen is frequently noted in individuals with compromised renal function receiving these drugs. Secondly, although fresh tetracycline compounds are not nephrotoxic, their oxidative degradation products (anhydro and epianhydrotetracycline) produce a toxic but reversible Fanconi syndrome[16] which is associated with changes in the distal renal tubules. Features of this syndrome include: polyuria, proteinuria, renal tubular acidosis, glycosuria, aminoaciduria and phosphaturia. Scattered reports,[17, 18] suggest a third problem, i.e., nephrogenic diabetes insipidus occasionally follows administration of demethylchlortetracycline.

THE PENICILLINS: The penicillins and cephalosporins are major divisions of the same chemical family. Drugs in both divisions produce ischemic renal dysfunction during anaphalaxis. Accentuation of azotemia is reported in individuals with prior renal impairment receiving either ampicillin or cephalothin but overt renal failure has not occurred.[19]

There are at least 35 reported cases of immune oliguric nephropathy beginning eight to 46 days after commencement of treatment with large doses of penicillin G and methicillin.[20] The signs of nephropathy include gross hematuria, sterile pyuria and azotemia preceded or accompanied by fever, skin rashes and eosinophilia. A variety of pathologic lesions such as glomerulitis, periarteritis and scattered areas of tubular necrosis or interstitial nephritis have been attributed to these drugs. Because of the association of such reactions with large and sustained doses of penicillin or methicillin, Baldwin postulates that the penicilloyl hapten may normally cross react or couple to structural renal proteins if the hapten is present in sufficient concentration.[20]

Among the penicillin family of antibiotics, only cephaloridine is associated with direct cytotoxic renal failure. Contributing factors such as excessive dosage, use of other nephrotoxic drugs, simultaneous use of diuretics and hypersensitivity reactions may play some role.[21] In animals, both furosamide and ethacrynic acid enhance the nephrotoxic action of cephaloridine.[22, 23] Clinically, azotemia is accompanied by proteinuria and cast formation. The histologic lesion is compatible with acute tubular necrosis of the proximal nephrons due to local concentration of reabsorbed cephaloridine.[24]

AMPHOTERICIN B: This potent systemic antifungal agent may initiate cytotoxic, immune or ischemic responses which adversely affect the kidney. Signs of cytotoxicity include urinary casts, proteinuria, glycosuria, hyposthenuria, renal tubular acidosis, azotemia, hyponatremia, hypokalemia and hypomagnesemia.[25] More than 80 percent of individuals receiving amphotericin B will develop some signs of toxicity during therapy and the depressed glomerular function, impaired renal blood flow or defective renal tubular function may persist after treatment.[5] Some signs of renal dysfunction may be related to the intense systemic vasoconstrictive response which accompanies intravascular administration of amphotericin B.

Renal biopsies show calcium deposits in areas of proximal and distal tubular degeneration. Histologic evidence of drug hypersensitivity includes interstitial inflammation. necrotizing vasculitis and glomerulitis.

THE SULFONAMIDES: Renal damage continues to be the most frequent serious complication of sulfonamide administration.[26] Crystalline concretions, obstructing the lumen of the nephron and producing necrosis of the distal renal tubule, follow administration of poorly soluble sulfonamide compounds such as sulfathiazole, sulfapyridine or sulfadiazine. The associated clinical features include crystalluria, hematuria, pyuria, cylinduria, renal colic, azotemia and oliguria.

Renal tubular necrosis with oliguria may occur in the absence of crystal formation. All of the sulfonamide derivatives may initiate hypersensitivity reactions with resultant glomerulitis, intrarenal arteritis or tubulointerstitial nephritis in the susceptible patient.

NEPHROPATHY AND THE INHALATION ANESTHETIC METHOXYFLURANE

Transient antidiuresis is anticipated following exposure to general anesthetic agents.[27] In contrast, more than 100 cases of a syndrome characterized by antidiuretic hormone resistant polyuria, dehydration, hemoconcentration, azotemia and renal oxalosis are reported among individuals receiving the inhalation anesthetic methoxyflurane (Penthrane).[28-40] Although the specificity of the syndrome to methoxyflurane is questioned,[29, 41] the observed incidence in a recent prospective study is 100% among patients receiving excessive amounts.[40]

Methoxyflurane is a highly lipid soluble dichloro-difluoroethylmethyl ether readily concentrated in the body fat depots. The total dose of the anesthetic, patient corpulence, pre-existent renal dysfunction and co-existing administration of other nephrotoxic drugs are mentioned as factors promoting development of the syndrome. Taves and associates[42] postulate that the polyuria is due to a direct toxic effect upon the distal renal tubule from inorganic fluoride, one of the metabolic products of methoxyflurane. Continued production of fluoride ions during release of the organic metabolites of methoxyflurane from the tissue lipids could account for persistence of the syndrome. The intratubular calcium oxalate crystals may simply represent the condensation products of oxalic acid, another metabolite of methoxyflurane.

Recovery from the syndrome after one or two weeks is the rule if the patients are adequately rehydrated. However, prolonged renal dysfunction with residual azotemia[28] and at least 20 deaths are reported.[29, 30, 32, 34, 37, 38]

SUMMARY

Drug related iatrogenic renal disease is most likely to occur with administration of cytotoxic agents preferentially excreted in the urine. The greatest risk of adverse renal drug reactions occurs with administration of multiple agents acting on the kidney and in those patients with pre-existing or co-

existing non-drug related nephropathy.

Azotemia with oliguria or a nephrotic syndrome are the common presenting features of many drug induced renal diseases. Polyuria, the Fanconi syndrome, and signs of interstitial nephritis (pyelonephritis) also may indicate iatrogenic renal disease related to pharmaceutical agents.

It is fortunate that most of the renal disorders produced by the drugs included in the present discussion are reversible if the signs of renal dysfunction are recognized early and the offending agents discontinued. Only with awareness of the potential complications of therapy and expectant observation for signs of renal dysfunction will the true incidence of drug related renal diseases become known. □

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the 3 phases of Eve



All women are not equal in their endogenous hormonal output. And, while all oral contraceptives are fundamentally effective, they exhibit **differences in their activity levels and estrogen-progestogen ratios that affect different women differently**—in both short and long-term use. Some brands may be insufficient for the woman's needs or else may exceed them.

Searle offers a family of O.C. products that covers the range of women's needs to help you provide the right pill for the right woman at the right time.

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the Ovulen phase

Most women* with a **balanced hormone profile and normal menses** do best on a middle-of-the-road pill that is neither estrogen dominant nor strongly progestogen dominant.

(*Typical clues—normal body build and breasts, feminine appearance, healthy skin and hair. Vaginal cytology slide—balanced "pink and blue.")

Some women having problems on other O.C.s might do well on Ovulen.

Ovulen has a distinctive hormonal balance that combines moderate estrogenic activity with a slight progestogen dominance. It has an excellent record of patient acceptance.

Ovulen®

Each white tablet contains: ethynodiol diacetate 1 mg./mestranol 0.1 mg.

SEARLE

For brief summary of prescribing information, see following page.



the Demulen phase

Many women* who secrete **more estrogen** than most do well on a pill with lower estrogen activity and an increased progestogen overbalance.

(*Typical clues—shorter, plumper, full-breasted, with glowing skin and no wrinkles. Vaginal cytology slide "pink.")

Some women with special conditions that may be aggravated by higher estrogen-activity products may do better on this ratio.

Demulen combines minimal estrogenic activity with a moderate ratio of progestogen overbalance. It is particularly well suited to the young when low-dose (activity) is preferred. Demulen offers little risk of the most potent progestogen side effects; early breakthrough bleeding is often transient.

Demulen®

Each white tablet contains: ethynodiol diacetate 1 mg./ethinyl estradiol 50 mcg
Each pink tablet in Ovulen-28® and Demulen®-28 is a placebo, containing no active ingredients.
Both Ovulen and Demulen are available in 21- and 28-pill schedules.

the Enovid-E phase

Some women* who secrete **less estrogen** than most do best on a pill with a moderate estrogen overbalance.

(*Typical clues—oily complexion, acne, hirsutism, masculinity, flat chest. Vaginal cytology slide—"blue.")

Patients with estrogen deficiency may show:

premenopausal syndrome
early-cycle bleeding
scanty menses
intermittent depression
increased appetite
steady weight gain
vaginal candidiasis

Enovid-E not only provides increased estrogenic activity with low progestogen activity, but also contains the only progestogen that is not antiestrogenic. Therefore it offers less risk of high-dose progestogen side effects.

Enovid-E®

Each tablet contains: norethynodrel 2.5 mg./mestranol 0.1 mg.

Oral contraceptives are complex medications and, after reference to the prescribing information, should be prescribed with discriminating care.

for the 3 phases of Eve:

a family of O.C. products

Ovulen®

Each white tablet contains:
ethynodiol diacetate 1 mg./mestranol 0.1 mg.

Demulen®

Each white tablet contains:
ethynodiol diacetate 1 mg./ethinyl estradiol 50 mcg.

Each pink tablet in Ovulen-28® and Demulen®-28 is a placebo, containing no active ingredients.

Actions—Ovulen and Demulen act to prevent ovulation by inhibiting the output of gonadotropins from the pituitary gland. Ovulen and Demulen depress the output of both the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH).

Special note—Oral contraceptives have been marketed in the United States since 1960. Reported pregnancy rates vary from product to product. The effectiveness of the sequential products appears to be somewhat lower than that of the combination products. Both types provide almost completely effective contraception.

An increased risk of thromboembolic disease associated with the use of hormonal contraceptives has now been shown in studies conducted in both Great Britain and the United States. Other risks, such as those of elevated blood pressure, liver disease and reduced tolerance to carbohydrates, have not been quantitated with precision.

Long-term administration of both natural and synthetic estrogens in subprimate animal species in multiples of the human dose increases the frequency of some animal carcinomas. These data cannot be transposed directly to man. The possible carcinogenicity due to the estrogens can be neither affirmed nor refuted at this time. Close clinical surveillance of all women taking oral contraceptives must be continued.

Indication—Ovulen and Demulen are indicated for oral contraception.

Contraindications—Patients with thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia and undiagnosed abnormal genital bleeding.

Warnings—The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis). Should any of these occur or be suspected the drug should be discontinued immediately.

Retrospective studies of morbidity and mortality conducted in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis, pulmonary embolism, and cerebral thrombosis and embolism and the use of oral contraceptives. There have been three principal studies in Britain[1-3] leading to this conclusion, and one[4] in this country. The estimate of the relative risk of thromboembolism in the study by Vessey and Doll[3] was about sevenfold, while Sartwell and associates[4] in the United States found a relative risk of 4.4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as nonusers. The American study also indicated that the risk did not persist after discontinuation of administration and that it was not enhanced by long-continued administration. The American study was not designed to evaluate a difference between products. However, the study suggested that there might be an increased risk of thromboembolic disease in users of sequential products. This risk cannot be quantitated, and further studies to confirm this finding are desirable.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions medication should be withdrawn.

Since the safety of Ovulen and Demulen in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period.

A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant cannot be determined at this time.

Precautions—The pretreatment and periodic physical examinations should include special reference to the breasts and pelvic organs, including a Papanicolaou smear since estrogens have been known to produce tumors, some of them malignant, in five species of subprimate animals. Endocrine and possibly liver function tests may be affected by treatment with Ovulen or Demulen. Therefore, if such tests are abnormal in a patient taking Ovulen or Demulen, it is recommended that they be repeated after the drug has been withdrawn for two months. Under the influence of progestogen-estrogen preparations preexisting uterine fibromyomas may increase in size. Because these agents may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. In breakthrough bleeding, and in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginam adequate diagnostic measures are indicated. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. Any possible influence of prolonged Ovulen or Demulen therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Ovulen or Demulen therapy. The age of the patient constitutes no absolute limiting factor, although treatment with Ovulen or Demulen may mask the onset of the climacteric. The pathologist should be advised of Ovulen or Demulen therapy when relevant specimens are submitted. Susceptible women may experience an increase in blood pressure following administration of contraceptive steroids.

Adverse reactions observed in patients receiving oral contraceptives—A statistically significant association has been demonstrated between use of oral contraceptives and the following serious adverse reactions: thrombophlebitis, pulmonary embolism and cerebral thrombosis.

Although available evidence is suggestive of an association, such a relationship has been neither confirmed nor refuted for the following serious adverse reactions: neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea during and after treatment, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately post partum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals and mental depression.

Although the following adverse reactions have been reported in users of oral contraceptives, an association has been neither confirmed nor refuted: anovulation post treatment, premenstrual-like syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption and itching.

The following laboratory results may be altered by the use of oral contraceptives: hepatic function: increased sulfobromophthalein retention and other tests; coagulation tests: increase in prothrombin, Factors VII, VIII, IX and X; thyroid function: increase in PBI and butanol extractable protein bound iodine, and decrease in T^3 uptake values; metyrapone test and pregnanediol determination.

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norethynodrel 2.5 mg./mestranol 0.1 mg.

Actions—Enovid-E acts to prevent ovulation by inhibiting the output of gonadotropins from the pituitary gland. Enovid-E depresses the output of both the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH).

Indication—Enovid-E is indicated for oral contraception.

The *Special Note, Contraindications, Warnings, Precautions* and *Adverse Reactions* listed above for Ovulen and Demulen are applicable to Enovid-E and should be observed when prescribing Enovid-E.

SEARLE **Enovid-E®**

brand of norethynodrel with mestranol

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Where "The Pill" Began

The Kidney Lymphatics: An Overview

A. T. K. COCKETT, MD
A. P. ROBERTS, BA

Kidney lymph, thought to be non-existent by some and not important by others, is evaluated. The anatomy and physiology with clinical application is emphasized. Treatment of pyelonephritis can not be fully appreciated without prior knowledge of renal lymphatics.

RENAL LYMPH is derived from kidney interstitial fluid and represents a combination of tubular reabsorbate and post glomerular capillary filtrate.

In the region of the outer cortex, renal lymph or interstitial fluid, will contain solutes which are found in higher tissue concentrations, whereas in the medulla the relatively increased water content in the intercellular environment will not only increase hilar lymph flow, but will lower the concentration of many solutes. Exceptions to this generalization are the higher concentration of potassium, renin and other selected antibacterial agents found in medullary lymph fluid.

ANATOMY OF INTRA-RENAL LYMPHATICS

We have confirmed the presence of two intra-renal lymphatic networks in the canine kidney.[1] Contrary to a previous report, the renal lymphatics accompany the venous system and branch in a fashion resembling the venules as they interconnect to form larger vessels.[2] The lymphatic network transports fluid in two directions. Lymph from the outer cortex is carried to the capsular region. Lymph from the juxta-medullary region and inner cortex probably courses in two divergent directions. Most of the intercellular fluid is transported via the medulla. This fluid emerges at the hilum. The remainder is transported to the capsular lymphatic system. The canine kidney resembles man in this peculiar way. Apparently, sheep and cows do not have a capsular lymphatic system or a medullary lymphatic network respectively.

SELECTED PHYSIOLOGIC STUDIES OF THE LYMPHATICS

Oxygen tension in the parenchyma of the kidney has been determined by analyzing lymph fluid. Details of this study have been published previously.[3] Mean oxygen tension of capsular renal lymph in dogs was 78 mm of Hg, whereas hilar lymph oxygen tension was 60 mm of Hg. This difference is significant. During these periods, arterial PO_2 was approximately 100 mm of Hg. These findings suggest that hilar lymph fluid may in all probability transport fluid with a lower PO_2 than what has been reported, since lymph fluid in this region represents an admixture of cortical and medullary fluid.

Glucose levels were determined in capsular and hilar lymph.[4] Glucose was elevated in the cortex (105 mg% compared to hilar

From the Division of Urology, University of Rochester School of Medicine and Dentistry, Rochester, New York.

lymph 90 mg%) suggesting that tubular reabsorption includes eventual egress of glucose into lymph and blood capillaries. Plasma level of glucose was 95 mg% during these periods. Hilar lymph levels of glucose were significantly lower ($P = < .01$) than capsular lymph concentrations.

Probenecid has recently been injected into the renal artery of canine kidneys before and after obtaining capsular and hilar lymph. An immediate and sustained elevation in para aminohippurate (PAH) was found after probenecid administration.[5]

CLINICAL CONSIDERATIONS

Renin has been analyzed in renal lymph.[6] Higher concentrations of renin-angiotensin were observed in hilar lymph than in capsular lymph. Total lymph flow, however, is markedly reduced when compared to total renal venous flow. The higher lymph concentrations of renin in lymph, when compared to equal volumes of renal venous plasma, cannot be of major significance systemically. Renin is converted to the vasopressor agent angiotensin by the substrate present in the interstitium. Under these conditions renin may play a role in regulating flow through the nephron.

Antibacterials in the Renal Interstitium—Kidney Lymph:

Since lymphatic capillaries drain the interstitium, concentrations of selected antibiotics found in lymph would have some bearing on the therapeutic response of that kidney during infection. We have emphasized the importance of achieving renal interstitial or lymph levels in the past. Urine levels or blood levels are less important.

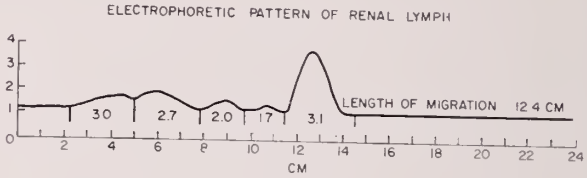
We have concerned ourselves with numerous patients who develop pyelonephritis. We believe that the ascending route via the bladder and lumen of the ureter is of primary importance. If partial obstruction is present, then pyelolymphatic backflow may occur.

We are impressed by the above mentioned sequence of events and would emphasize that many cases of kidney infection begin initially as an interstitial lymphangitis. Renal lymph will suppress bacterial growth. We have determined the concentration of protein in canine renal lymph (Table 1). Gamma globulin is present. Normal renal lymph also has many small lymphocytes.[7]

PROTEINS IN RENAL LYMPH AND PLASMA

	RENAL LYMPH		PLASMA	
	GRAM %	% TOTAL	GRAM %	% TOTAL
TOTAL PROTEINS	0.3		8.1	
ALBUMIN	0.13	49	2.7	33
ALPHA-1	0.02	6	0.1	2
ALPHA-2	0.4	12	0.3	4
BETA	0.06	19	1.0	11
GAMMA	0.5	14	4.0	50

Table 1. Content of protein in kidney lymph.



If an antibacterial agent can be found in higher levels in renal lymph than in blood, during the same interval, then this agent will be effective in eradicating acute episodes of pyelonephritis. The offending organism must be sensitive to the appropriate antibacterial agent which must suppress growth in the test tube at levels which can be achieved in tissue spaces. Of some importance is the fact that these lymph levels should be achieved when the agent is infused or administered orally in non-toxic, therapeutic doses.

Penicillin G has been evaluated because investigators have advocated its use in common urinary infections caused by *E. coli* and related gram negative organisms. When

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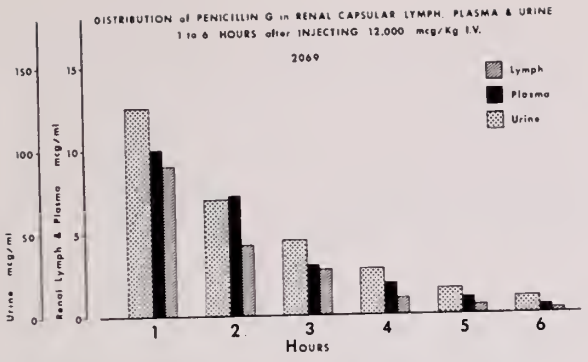


Figure 1. Distribution of penicillin G in renal capsular lymph, plasma and urine, after intravenous injection.

penicillin G is injected intravenously in a bolus, the distribution of this antibiotic can be determined (Figure 1). We have also infused penicillin G at a constant rate. Figure 2 illustrates the distribution of the antibiotic when blood levels are sustained. Evidence of back-diffusion from the tubular lumen to the interstitium is not seen. We have mentioned the injection of probenecid and its effect on PAH in renal lymph (Figure 3). We believe that penicillin G would also behave in similar fashion.

Cephalothin (46 mg/kg) has been given to dogs by the intravenous route. The typical distribution of this antibiotic in the renal lymph is illustrated (Figure 4). Cephalothin and penicillin G appear to be transported and excreted in similar fashion by the kidney.

The antibiotic cephaloridine, however, is distributed somewhat differently in renal lymph (Figure 5). The lymph concentrations exceed corresponding blood levels. Actual nephrotoxicity may simply represent significantly higher concentrations in the renal interstitium. We believe that maximal levels should be demonstrated in hilar lymph since this network drains the medulla.

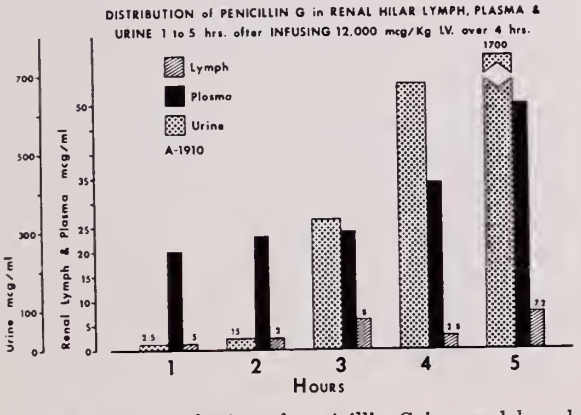


Figure 2. Distribution of penicillin G in renal lymph and plasma after sustaining blood levels by infusion pump.

Effect of Probenecid on Renal Lymph Transport of PAH

Source of Sample	Control	40mg/kg Probenecid	
Capsular Lymph / Arterial Plasma	0.47 ± 0.07 (16)	0.73 ± 0.11 (24)	P = < 0.001
Hilar Lymph / Arterial Plasma	0.52 ± 0.8 (17)	0.67 ± 0.11 (25)	P = < 0.001

Figure 3. Effect of probenecid (40 mg/kg) on renal lymph levels of para-aminohippurate (PAH). Values are expressed as a ratio (lymph/artery).

The second antibacterial which has renal lymph concentrations exceeding corresponding plasma levels is nitrofurantoin.[8] We have evaluated renal lymph containing nitrofurantoin in dogs. The lymph concentrations with this agent will suppress growth of *E. coli*.[8] While this antibacterial effects low blood levels, it is effective in the urinary tract because of high urinary concentrations.

Cephalexin, a new antibiotic, has been evaluated in dogs. From published reports approximately 80% of this agent is excreted via the kidneys. This antibacterial also is, for practical purposes, not bound to serum protein. Serum concentration studies above 1 mg/ml indicate that cephalothin is approximately 25% bound, while only 10% of cephalexin is bound.

In Figure 6 renal capsular lymph, hilar lymph and blood concentrations were plotted in four dogs. Cephalexin was given intravenously as a bolus (10 mg/kg). The concentrations in the kidney medulla and cortex one to four hours after injections are

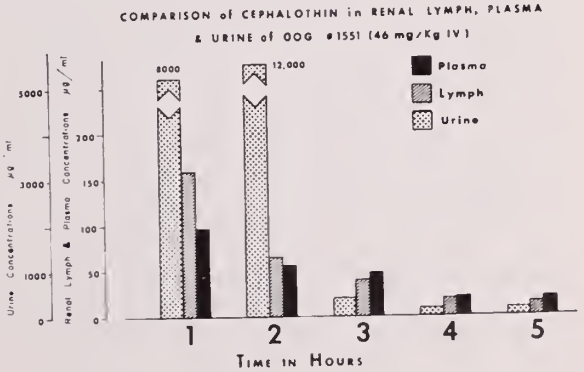


Figure 4. Distribution of cephalothin in renal lymph, plasma and urine. Single canine experiment.

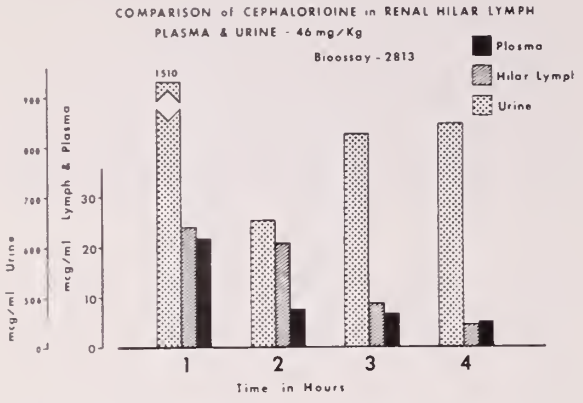


Figure 5. Distribution of cephaloridine in renal lymph, plasma and urine. Single illustrative experiment.

shown. Initially, capsular and hilar lymph levels exceed the serum levels. During the next several hours, blood levels are maintained while a gradual reduction in lymph levels is observed.

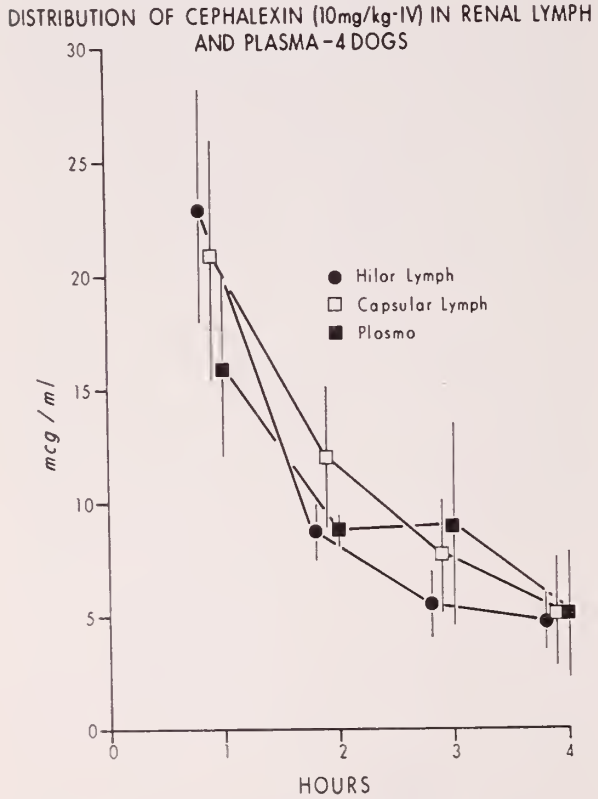


Figure 6. Distribution of cephalexin in renal capsular lymph, hilar lymph and plasma. Average of values from four dogs.

From published data, it is worth mentioning that probenecid does not increase the blood levels of cephaloridine after its administration. Thus it would appear that cephaloridine is filtered by the glomeruli and is reabsorbed by the proximal tubules in significant concentrations.

SUMMARY AND CONCLUSIONS

These selected studies do not represent a complete review. Instead we believe that they bring together in a biased fashion our widely published reports covering a ten-year period. These studies support several basic themes:

1. The lymphatics play an important role in the fluid transport of electrolytes, enzymes and antibacterials.

2. If significant concentrations of antibacterials can be achieved in the lymph—exceeding blood concentrations—the susceptible kidney infection probably will be eradicated.

3. During periods of urinary obstruction, the lymphatics act as a safety valve. In this instance antibacterials in significant concentrations can be transported by the lymph.

At some future date a more comprehensive review will be published. We are presently embarked on a program to publish a monograph on the kidney lymphatics, an active fluid transport system. □

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260 Crittenden Boulevard, Rochester, New York 14642

The Quality of Success in the Treatment of Cancer

JOHN E. HEALEY, Jr., MD

Previously, little effort was made to rehabilitate the cancer patient. Today with the quantity of success it becomes necessary to consider the quality of success.

I BELIEVE that it is best to start any discussion by a definition of terms. There are two terms of significance in the title of this discussion, "rehabilitation" and "cancer." The term rehabilitation is derived from the French word "rehabilitare" which means "to make suitable again." This is a good term. It is clear, concise, and comprehensible. Cancer is derived from the Latin word "cancri" which means "crab." Cancer is a bad term. It is completely non-descriptive and it carries with it a very ominous connotation. Probably the best thing that could happen to cancer patients would be for us to abandon the name cancer and substitute another. Hansen's disease, for example, is much more acceptable to the public and physicians alike than is "leprosy." But the abandonment of the term cancer is beyond hope and we're stuck with it. We can only strive to educate the public and physicians as to the results of cancer treatment which prove that cancer patients do have a rehabilitation potential.

Presented before the Symposium on The Care of Head and Neck Cancer Patients and Their Rehabilitation. Sponsored by the Tulsa area Cancer Control Program and the Oklahoma Regional Medical Program, January 23rd, 1970, Tulsa, Oklahoma.

Up until three years ago the primary goals in clinical cancer research were to develop better methods for early diagnosis and to refine the methods of definitive treatment. These goals were deserving, of course, because the success of cancer treatment is determined by longevity. These research endeavors were directed toward the improvement of the quantity of success and this increased *quantitative* success is being realized. But what was lacking was a *qualitative* analysis of the survival of these patients.

Why this lack of interest in the quality of survival? I think that it stems primarily from the pessimistic, the defeatist, and, in fact, the fatalistic attitude toward these cancer patients by the laity, by the paramedical groups and by physicians alike. We have been emphasizing our failures rather than our successes.

It is easy to understand why the laity possess this fatalistic feeling toward cancer. They hear nothing but publicity given to the fatalities amongst celebrities affected by cancer. The public hears the fear tactics used by the Cancer Society and the insurance companies. But what has not been emphasized to the public is the great progress that has been made over the years in the management of patients with cancer. In the early 1900's, for example, few patients had any hope for cure. Today, as estimated by the American Cancer Society, one of every three cancer patients has his disease controlled. The public is unaware of the fact that there are approximately 2,000,000 persons living today cured of their disease. The public is poorly informed of the decrease of advanced stages of cancer in certain ana-

TABLE I

CANCER OF THE CERVIX

Cases Primarily Treated at M. D. A. H.

Squamous Cell by Stage, by Year of Admission

3/44 - 8/68

YEARS	IN-SITU, %	STAGE, % I	II	III	IV
3/44-8/49	1.8	13.6	36.1	33.1	15.4
9/49-8/54	4.6	12.4	49.7	30.0	3.3
9/54-8/59	10.4	16.5	32.0	36.5	4.6
9/59-8/64	21.8	22.4	29.5	21.6	4.7
9/64-8/68	27.4	23.2	27.5	19.0	2.9

Total Number of Cases = 4,296

tomical areas. Table I, for example, shows the changes in the incidence of the various stages of cancer of the cervix from 1944 through 1968 in cases primarily treated at The University of Texas M. D. Anderson Hospital. From this table one can see the decrease in incidence of the more advanced cases (Stages III and IV). More significant is the increase in the earliest stage, carcinoma in-situ, from 1.8% in 1944-49 to 27.4% in 1964-68. These figures reflect the value of public education regarding the importance of early diagnosis.

Unfortunately, physicians also maintain a pessimistic attitude toward rehabilitation of the cancer patient. This feeling is due to several factors in the physician's education. He is given very poor exposure to cancer in his medical curriculum. What the medical student does get is fragmentary, *i.e.*, each specialty group will discuss cancer as it affects a specific anatomic site. The cancer patient in a university hospital to whom the student is exposed is usually an advanced or terminal case. Rehabilitation is not even considered, let alone discussed with the student. There is rarely an attempt to present to him the basic concepts of oncology. The medical student's exposure to the basic concepts of rehabilitation is even more lacking. Rehabilitation medicine unfortunately is equated by the physician to physical medicine. Whatever term is used it is merely an elective for the student and rarely elected. As a result, the average practicing physician has little knowledge as to what rehabilitation is all about.

The paramedical groups alho have the same fatalistic attitude regarding cancer that any lay person possesses but in addition they are exposed to the pessimism of the physicians with whom they associate. This results in even greater pessimism in this group. We have had a great deal of difficulty in the past years in recruiting physical and occupational therapists. At one school of physical therapy graduates were told not to bother to apply at M. D. Anderson Hospital because "there is nothing you can do for these patients." The same was true in recruiting nurses. The rehabilitation and vocational agencies in the nation also have been remiss. Up until three years ago, we could not get any type of appliance for the medically indigent cancer patient from any of the vocational agencies unless we waited 18 months and the patient had no evidence of metastasis. Here was almost two years lost from their lives without any recourse to rehabilitation, either physical or vocational. Even at the end of 18 months with the cancer controlled and with no evidence of metastasis the stigma of cancer remained and we still do not get assistance.

At present this attitude has changed. It has changed primarily because a significant increase has been made in the quantity of success in this group of patients. This increase is due to a number of factors: public education for one. The danger signals put out by the cancer society have obviously been helpful in some instances but in our own institution fear is still the main reason for the delay in seeking medical treatment. Many new therapeutic methods have been added to our armamentarium. In the triad of therapeutic approach, there are new and better radical surgical procedures, great ad-

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John E. Healey, Jr., MD, who graduated from Jefferson Medical College in 1948, limits his practice to Rehabilitation Medicine. He is Professor of Rehabilitation Medicine at the M. D. Anderson Hospital in Houston and Professor of Anatomy at the Graduate School of Biomedical Science at the University of Texas in Houston. He is a member of the American Congress of Rehabilitative Medicine, the National Rehabilitative Association and the American Association of Anatomists.

TABLE II

PHYSICAL RESTORATION PROGRAMS

FACIAL DISFIGUREMENTS
SHOULDER DYSFUNCTION
LYMPHEDEMA
AMPUTATIONS
SPEECH DEFECTS (LARYNGECTOMY)
NEUROLOGICAL DEFICITS
STOMAS (TRACHEAL, PHARYNGEAL, ILEOSTOMIES, COLOSTOMIES, ILEAL CONDUITS)

vances in radiotherapy, and many new chemotherapeutic agents. We now have the increased usage of the combination of these various modalities of treatment. This has all resulted in an increase in the control of cancer but it has also changed the terminal stage of the disease. Regardless of the modality used—radiation, surgery, or chemotherapy—certain physical changes may result which can cause problems in rehabilitating the patient. Table II lists some of the major physical restorative programs that we have underway. A regional maxillofacial restorative center has been formed with help from the social and rehabilitative services of the Department of Health, Education and Welfare. The center is headed by Doctor Joe Drane and serves those patients with facial disfigurements resulting from surgical removal of head and neck tumors. The treatment of shoulder dysfunctions resulting from radical neck dissection and radical mastectomy is an important physical restoration activity. Lymphedema of the extremities is a common and frequently ignored problem in the cancer patient. Amputation of an extremity may be required in the treatment of tumors of bone or soft tissues of the limb. Speech therapy is needed for many patients subjected to operative procedures in the oral, pharyngeal or laryngeal cavities. Neurological defects may result from invasion of the central or peripheral nervous system. Important peripheral motor nerves must be sacrificed at times in order to extirpate a lesion. Radiation fibrosis may affect the central or peripheral nervous system or neurotoxic effects may result from the administration of certain chemotherapeutic drugs used to combat cancer. Stomas are quite frequent occurrences in the cancer patient. So common, in fact, that a new paramedical specialty has been



Figure 1

formed, the enterostomal therapist, to assist these patients. These are but a few of the many physical problems important in the rehabilitation of the cancer patient.

As already mentioned, in past years we could not get an artificial limb for cancer patients until 18 months postoperative, but we can now get assistance even for immediate fitting of a prosthesis. We have a number of patients with temporary artificial limbs fitted at the operating table, as shown in Figure 1. This picture was taken 48 hours following the amputation. One month later this young lady was back in school with her permanent prosthesis.

Now, despite the awareness of the needs for physical restoration, the qualitative success is still lacking. We have very little documentation as to how these patients adjust to their disease, how they are accepted by their families, friends, community, vocations, and how they are affected economically. We can cite specific cases and speak in generalities but the documentation is still lacking.

I think anyone who speaks of the rehabili-

tation of cancer patients would be remiss if he did not mention the name of the late Miss Mary Switzer, former Administrator of the Department of Health, Education and Welfare's Social and Rehabilitation Service. It was through her individual efforts that this change of philosophy came about. The significance of this was the impact primarily on financing, as she put forth the doctrine that cancer patients should be considered as having a rehabilitation potential. This doctrine is reflected not only in those medically indigent patients but in many other areas as well.

We are often asked what is the rehabilitation potential of, for example, a particular individual with a particular type of tumor. We always have to say it is an individual thing. As an example, I can cite the story of two brothers who lived in a little town in East Texas who were highly regarded by their community. They were clean living kids and were the sole support of a mother and three sisters. One brother, Joe, had an unfortunate accident which required the amputation of an extremity above the elbow. Almost immediately, the town folks took up a collection to alleviate the boy's financial situation. He was eligible for Workmen's Compensation and a politician, not a physician, referred him to the Texas Division of Vocational Rehabilitation. At the proper time he was fitted with an artificial limb, given job training and placement. He ended up much more economically sound than he was prior to his accident. About a year and a half later, his brother, Cornelius, noticed a lump in his wrist and he was sent to the hospital where a diagnosis of chondrosarcoma was made. This required an amputation of the upper extremity above the elbow. There was no fund raising for Cornelius because he had the "Big C," and it was felt that he would not be around long enough to utilize this money. He was not eligible for Workmen's Compensation and, at this time, the Division of Vocational Rehabilitation would not accept cancer patients because of the poor rehabilitation potential.

So, here we have two brothers, each with a similar physical deformity. Joe, a trauma victim, was completely rehabilitated, and Cornelius, a cancer victim, was given no rehabilitation and, although he hated to do it, he had to depend on charity through the welfare program.

The gist of the story is this. About two years following the initial injury, Joe had another accident. You might say that he was accident prone. It was a fatal automobile accident. Cornelius, now eight years postoperative, without evidence of disease, is still collecting welfare money, your money and mine. In essence, the main purpose of rehabilitation agencies in this country is to try to get physically handicapped patients into a wage earning position.

So now we realize that with the cancer patient we must go beyond the definitive treatment and consider his total rehabilitation. Total rehabilitation requires a great team effort, including many paramedical groups. *Rehabilitation is considered the fourth phase of medicine.* The first is prevention, the second is diagnosis, third is definitive treatment, and the fourth is rehabilitation.

Although rehabilitation medicine is new in practice, it is certainly not new in theory. I would like to cite a quotation, "The great majority of patients seriously ill can be rehabilitated. With the physician calling to his aid various specialists, he is able to bring relief to a large number of patients who formerly were looked upon as beyond help. *Rehabilitation is to be a master word in medicine.*" (Italics mine.) The quotation was not made by any of our contemporaries but by Dr. William Mayo in 1925.

As physicians, perhaps we have made a grave mistake in regard to the cancer patient. We have attempted to cure the disease, but cancer, as many agree, is a group of chronic diseases. We do not entertain a cure for other chronic diseases. We don't cure arteriosclerotic heart disease. We don't cure arthritis. We don't cure diabetes, and we don't cure hypertension but we do control, or arrest, these diseases. This same type of control should be the goal of cancer treatment. Cancer patients should be considered in the same category as other chronic disease patients and given the same rehabilitation efforts.

It is difficult to assess the rehabilitation potential of cancer patients since funds have

TABLE III

STATE OF TEXAS DVR CLOSURE BY DISABILITY
1967-1968 FISCAL YEAR

DISABILITY	COST FOR REHABILITATED CLOSURES	TOTAL CASES SERVED	REHABILITATED CLOSURES	PERCENT CLOSURES
Orthopedic Deformities	1,253,865	10,357	1,631	10.5
Mental Retardation	830,443	6,362	1,852	29.3
Heart Disease	271,864	1,593	244	15.3
Tuberculosis	109,810	1,137	195	17.1
Diabetes	37,490	492	66	13.4
Cancer	15,579	142	42	29.5
All Disabilities	4,909,320	42,357	8,357	19.7

not been available to carry out a prospective study of this problem. One indicator is shown in Table III. This table lists a group of selected chronic disease states showing the number of total cases served in each category, as well as the number and percentage of rehabilitated closures and the cost for such closure during the fiscal year 1967-68. A rehabilitated closure refers to a client who has returned to a gainful employment or one who has removed his or her dependency upon other family members or welfare agencies (*i.e.*, a housewife who is now able to perform her household duties). From this table one can note that of the chronic diseases

TABLE IV

THE UNIVERSITY OF TEXAS M. D. ANDERSON HOSPITAL PATIENT REFERRALS TO DVR
1967 - 1969

TOTAL REFERRALS:	162	
No Closure Information:	40	
Closure Information:	122	
Rehabilitated Closure	—	73 (59.8%)
Not Rehabilitated	—	49 (40.2%)
Medical Reasons	—	40
Other Reasons	—	9

listed, cancer patients rate the highest in percent of closures. You will also note that they rate lowest in the number of patients served. However, cancer also rates first in the low cost per closure; $370.00 per closure as compared to $1,114.00 for the rehabilitation of the patient with heart disease. From our own institution, 162 patients were referred to the Division of Vocational Rehabilitation during the two-year period 1967-1969. Final closure information was obtainable on 122 of these patients. Of these 122 patients, 73 (59.8%) were rehabilitated closures. (Table IV)

These figures prove that the rehabilitation potential of the cancer patient is comparable to other chronic disease patients. The cancer patient should, therefore, be offered the same rehabilitation efforts as offered other patients with a chronic disease. We must continue to increase the quantity of success but be ever mindful that we must improve the *quality* of success as well. □

Texas Medical Center, Houston, Texas 77025

"DOCTOR,

IS YOUR CALENDAR MARKED FOR

MAY 18th, 19th, 20th, 1972?"

Reserve This Time to Attend Your

66th OSMA ANNUAL MEETING

SEE COMPLETE DETAILS ON

PAGE 153

News From The Oklahoma State Department of Health

STATE DENTAL HEALTH PROGRAM

Prevention, education and dental care make up the three facets of the Dental Health Service program at the State Health Department. Five staff dentists and two dental health educators work in assigned areas of the state.

The dental health education consists of classroom lectures for elementary school children; workshops and seminars concerning preventive dentistry for school teachers, nurses and others involved with the dental health of children; and the preparation and statewide distribution of dental health educational materials.

Community and school water fluoridation, plaque control programs, and topical fluoride applications for dentally indigent children make up the preventive program, in addition to referrals to private dentists of children found to need dental care. Restorations and extractions for selected dentally indigent children in areas of the state that have a shortage of dental manpower also form a part of the dental service's program.

In 1971, the Dental Health Service began a project to evaluate each of its major program areas by using the DMF (decayed, missing and filled teeth) index to measure change in the dental health status of Oklahoma's children. To accomplish this statewide evaluation survey, dental examinations were performed for 2,831 randomly selected elementary school children, and the dental caries experience of those students was recorded and analyzed according to their age, race and region of residence in Oklahoma.

The completed survey showed that children in the southeastern region of Oklahoma demonstrated both a higher dental caries experience, and a lesser amount of dental care received, than did children from other regions of the state. Black children in the survey showed a lesser amount of dental caries experience, and also a lesser amount of dental care received, than did the white and Indian children surveyed.

The average number of teeth affected by dental caries among all elementary school children in Oklahoma was found to equal 4.04 teeth per child. □

COMMUNICABLE DISEASES IN OKLAHOMA FOR FEBRUARY, 1972

Disease	February 1972	February 1971	January 1972	Total to Date 1972	Total to Date 1971
Amebiasis	3	9	1	4	13
Brucellosis	—	—	—	—	—
Chickenpox	39	19	37	76	43
Encephalitis, infect.	2	1	—	2	4
Gonorrhea	856	583	759	1615	1075
Hepatitis, infect. & serum	66	43	42	108	105
Leptospirosis	—	—	—	—	—
Malaria	—	4	—	—	21
Meningococcal infections	1	2	—	1	2
Meningitis, aseptic	3	3	1	4	7
Mumps	40	32	31	71	54
Rabies in animals	14	29	8	22	55
Rheumatic fever	9	1	1	10	4
Rocky Mt. spotted fever	—	—	1	1	1
Rubella	—	10	2	2	23
Rubella, congenital syn.	—	—	—	—	—
Rubeola	—	182	1	1	406
Salmonellosis	7	12	3	10	34
Shigellosis	4	9	1	5	24
Syphilis	126	82	80	206	218
Tetanus	—	—	—	—	—
Tuberculosis, new active	17	19	16	33	41
Tularemia	—	—	—	—	—
Typhoid fever	—	—	—	—	—
Whooping cough	3	1	1	4	4

ANNOUNCING THE 1972
OSMA ANNUAL MEETING

MEDICINE TOMORROW

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ANNUAL MEETING PROGRAM

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ANNUAL MEETING
TELEPHONE MESSAGE CENTER

ATTENTION:

While you are attending the OSMA Annual Meeting in Oklahoma City, your emergency calls may be referred to:

272-9231

A courtesy message center will be maintained by Southwestern Bell Telephone during the 66th OSMA Annual Meeting in the Skirvin Hotel Convention Center.

Oklahoma State Medical Association



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TRUSTEES

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Alternate (1973) Edward W. Allensworth, MD, Vinita

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District 3: Garfield, Grant, Kingfisher, Logan
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Alternate (1973) . . Robert J. Hogue, MD, Guthrie

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Alternate (1974) . . Y. E. Parkhurst, MD, Norman

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Trustee (1974) . . Jack L. Richardson, MD, Tulsa
Alternate (1974) William M. Benzing, Jr., MD, Tulsa
Alternate (1974) . . . Myra A. Peters, MD, Tulsa

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Alternate (1974) . . Burdge F. Green, MD, Stilwell

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Trustee (1974) . C. S. Cunningham MD, McAlester
Alternate (1974) . . Jack W. Parrish, MD, Seminole

District 11: Atoka, Bryan, Choctaw, Coal, McCurtain, Pushmataha
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1972 Annual Meeting Committee

John A. Blaschke, MD, Oklahoma City, General Chairman
Dale Groom, MD, Oklahoma City, Program Chairman

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Norman L. Bartlett, MD, Tulsa
Jake Jones, Jr., MD, Shawnee
E. C. Yeary, MD, Ponca City

Digest of Events

HOTEL ACCOMMODATIONS

Headquarters for the 66th Annual Meeting will be the Skirvin Hotel, Oklahoma City, where a large block of rooms have been reserved for members of the Oklahoma State Medical Association. Physicians are requested to make their own reservations by writing directly to the Skirvin Hotel, P. O. Box 1677, Oklahoma City, Oklahoma 73101 —providing the hotel with dates and times of arrival and departure.

REGISTRATION

General registration will be located on the second floor of the Skirvin Hotel inside the Convention Center. Hours will be from 8:00 a.m. until 5:00 p.m. on Thursday, Friday, and Saturday, May 18th-20th.

Members of the House of Delegates (including the Board of Trustees and Officers) may register starting at 8:00 a.m. on Thursday morning, May 18th, at the general registration desk. Registration for the House will be continued throughout Thursday.

The presentation of Delegate's credentials cards will be necessary to receive special badges and portfolios containing the business items to be considered.

BOARD OF TRUSTEES

The OSMA Board of Trustees will conduct its annual business meeting Wednesday, May 17th, starting at 5:30 p.m. in the Skirvin Hotel's Crystal Room. Dinner will be served.

HOUSE OF DELEGATES

The OSMA House of Delegates will conduct two sessions during the 1972 annual meeting. However, unlike past years, both sessions will be conducted on the same day, Thursday, May 18th.

The opening session will be held at 8:30 a.m. in the Skirvin Hotel's Convention Center on Thursday.

Reference committees will meet starting at 10:00 a.m. on Thursday morning on the second floor of the Skirvin Hotel immediately after the opening session of the House of Delegates. The closing session of the House of Delegates is scheduled for 7:30 p.m. Thursday evening in the Convention Center.

All items of business introduced during the opening session will be referred to the reference committees for hearing starting at 10:00 a.m. Open hearings on the reports and resolutions will be conducted by the four committees, providing all OSMA members with an opportunity to present their views.

The reference committees will prepare reports containing recommendations for presentation to the House of Delegates at its closing session Thursday evening. Elections will also be held during the closing session.

HOUSE OF DELEGATES DINNER

A special reception and dinner has been planned for the members of the House of Delegates and their guests starting at 5:00 p.m. in the Skirvin Tower Hotel's Persian Room. Featured speaker for the evening will be Max H. Parrott, MD, Portland, Oregon, Chairman of the American Medical Association's Board of Trustees. Attendance at the dinner is *not* restricted to members of the House of Delegates, any member of the association may attend. Dinner tickets are $5.00 each.

SCIENTIFIC SESSIONS

The scientific and educational portion of the annual meeting will be held on the second floor of the Skirvin Hotel on Thursday afternoon and all day on Friday and Saturday.

A complete program appears in this issue of *The Journal.*

MEET THE CANDIDATES LUNCHEON

An old fashioned "political speaking" will be held at 11:30 a.m. on Friday, May 19th. Ham hock and beans, salad, relishes, and dessert will be on the menu. Short talks will be given by the three front running candidates for Oklahoma's Junior Senator's Seat: Charles Nesbitt, Ed Edmondson, and Dewey Bartlett.

Due to a limitation on space, only 250 people will be able to attend. Although tickets are free, they are on a first come-first serve basis.

FREE PICNIC LUNCHEON

The proverbial free lunch will be offered to all physicians on Saturday when the Insurance Company of North America will host a picnic-type spread.

Corned beef and pastrami sandwiches, beer, soft drinks, assorted relishes and side dishes will be served in an informal atmosphere.

COCKTAILS ALFRESCO

Cocktails and music at poolside will be the

featured happening on Friday evening, May 19th. A free cocktail party will be held from 5:30 p.m. until 7:00 p.m. around the Skirvin Hotel's Sun Suite Swimming Pool. All OSMA members and their wives are invited to attend. Music will be provided by strolling mariachies.

CORONARY HEART DISEASE—1972

The scientific highlight of the annual meeting will take place at 1:30 p.m. on Friday afternoon, May 19th, when four outstanding teachers from the Mayo Clinic will present a symposium entitled "Coronary Heart Disease-1972." The four experts will conduct an in depth look into what is actually known about coronary heart disease, its causes, prevention and treatment. They will cover such topics as the role of monitoring, pacemakers, physical exercise, coronary arteriography and of surgery.

FUTURE OF MEDICINE

Medical practice is undergoing revolutionary changes that are being brought about not by scientific advancement, but by economic and sociological pressures. The future of medicine is being dictated by sources outside of the profession, sources quite often completely unfamiliar with either the scientific or personal aspects of medicine. At 1:30 p.m. on Saturday afternoon, May 20th, four nationally recognized opinion leaders will discuss and predict medicine's future. Max H. Parrott, MD, is the knowledgeable and articulate Chairman of the AMA Board of Trustees. Richard Wilbur, MD, is former Deputy Executive Vice-President of the AMA and now an Undersecretary in the U. S. Department of Defense. Wilbur J. Cohen, PhD, is one of the foremost social planners of the day and a principle architect of Medicare. Jenkin Lloyd Jones is Past-President of the U. S. Chamber of Commerce, Publisher of the Tulsa Tribune, and an internationally known syndicated columnist. All of these men are known for their intellect, knowledge, foresight, and especially for their forthrightness.

PRESIDENT'S INAUGURAL DINNER-DANCE

On Saturday night, May 20th, the annual President's Inaugural Dinner-Dance will be held at 6:00 p.m. in the Skirvin Tower Hotel's Persian Room.

Stanley R. McCampbell, MD, Oklahoma City, will succeed Lucien M. Pascucci, MD, Tulsa, as President of the OSMA. The inaugural ceremony will follow the banquet and entertainment.

Featured entertainment for the evening will be the nationally known Cry-Slurs of Northwest High School in Oklahoma City.

The banquet will feature a gourmet menu including tenderloin of beef complimented by red wine and Cherries Jubilee as dessert. During the dance—played by the popular Al Good Orchestra—setups will be provided.

Social hour, dinner with wine, inaugural ceremony, dancing and entertainment—a delightful evening—all for the below-cost price of $12.50. Order your tickets in advance from the OSMA, 601 N. W. Expressway, Oklahoma City 73118.

GOLF AND TENNIS TOURNAMENTS

The annual OSMA Golf Tournament will be held at the beautiful new Kickingbird Golf Course near Edmond, Oklahoma. Contestants may tee off anytime on Friday, May 19th, starting at 8:00 a.m. Trophies will be provided by the OSMA and winners will be announced at the President's Inaugural Dinner-Dance.

Tennis players will compete for OSMA trophies at the Will Rogers Memorial Tennis Center in Oklahoma City on Friday, May 19th, beginning at 12:00 noon. Men's singles and doubles will be played with consolation rounds for the first round losers. A wives' tournament is also being planned with singles and doubles competition. Winners will be announced and trophies awarded at the President's Inaugural Dinner-Dance. Entries should be sent in advance to Farris W. Coggins, MD, 5700 N. W. Grand Blvd., Oklahoma City, Oklahoma 73112.

PAST-PRESIDENTS' BREAKFAST

The traditional breakfast for Past-Presidents of the OSMA will be held at 7:30 a.m., Friday, May 19th, in the Skirvin Hotel's Crystal Room.

EXHIBITS

Primary financial support for the annual meeting will be provided by the technical exhibitors (see roster on page 163). The exhibit area, which will also feature scientific and institutional displays, will be in the Skirvin Hotel's Convention Center. Viewing hours will be 1:00 p.m. until 5:00 p.m. on Thursday, and 9:00 a.m. until 5:00 p.m. on Friday and Saturday.

PROGRAM

All Events Will Be in the Skirvin Hotel Unless Otherwise Noted

Wednesday Evening, May 17th

5:30 p.m. **BOARD OF TRUSTEES MEETING.** The annual business meeting of the Board of Trustees will be held in the Crystal Room of the **Skirvin Hotel.**

Thursday Morning, May 18th

8:30 a.m. **HOUSE OF DELEGATES MEETING.** The opening session of the House of Delegates will be held in the **Skirvin Hotel's Convention Center.**

10:00 a.m. **HOUSE OF DELEGATES REFERENCE COMMITTEE MEETINGS.** Four House of Delegates Reference Committees will hold open meetings on all business items in meeting rooms located on the second floor of the **Skirvin Hotel.**

Thursday Afternoon, May 18th

1:30 p.m. **PSYCHIATRY SECTION.** "Improving Patient Care in Psychiatry and its Socio-Economic Aspects." Speaker—Robert Gibson, MD, Sheppard and Enoch Pratt Hospital, Towson, Maryland.

1:30 p.m. **GOVERNMENTAL RELATIONS WORKSHOP.** Key Administrators of government health care programs will discuss program concepts, claims administration, profile determination and problem areas for the benefit of physicians, business managers and office assistants. In addition, a representative of the Economic Stabilization Program will discuss the wage and price freeze and its effect on physicians. Moderator—Mark R. Johnson, MD. Speakers—Daniel E. Morley, Aetna-Medicare Claims; Bertha M. Levy, MD, Department of Institutions, Social and Rehabilitative Services; Colonel E. V. Allen, CHAMPUS; Pete White, Economic Stabilization.

Thursday Evening, May 18th

5:00 p.m. **DELEGATES RECEPTION AND DINNER.** Members of the House of Delegates and other interested members of the OSMA are invited to this cocktail hour and dinner meeting featuring an address by Max H. Parrott, MD, Portland, Ore-

gon, Chairman of the Board of Trustees, American Medical Association. Dinner tickets are $5.00 each.

7:30 p.m. **HOUSE OF DELEGATES MEETING.** The closing session of the House of Delegates will be held in the **Skirvin Hotel's Convention Center.**

Friday Morning, May 19th

8:00 a.m. **OSMA ANNUAL GOLF TOURNAMENT.** The tournament will be held at the beautiful new Kickingbird Golf Course near Edmond. Trophies will be provided by the OSMA and winners will be announced at the President's Inaugural Dinner-Dance.

9:30 a.m. **PEER REVIEW SYMPOSIUM.** Congress is demanding sophisticated and comprehensive peer review programs to reduce utilization of government health care plans and to monitor the quality of medical services. Should organized medicine assume these review responsibilities? Moderator—Hillard E. Denyer, MD. Speakers—Joseph D. Wassersug, MD, Quincy, Massachusetts; F. William Dowda, MD, Atlanta, Georgia; Howard B. Keith, MD, Shattuck, Oklahoma.

11:30 a.m. **MEET THE CANDIDATES LUNCHEON.** This will be an old fashioned "political speaking" with ham hock and beans, salad, relishes and dessert. Short talks will be given by the three front running candidates for Oklahoma's Junior Senator's Seat: Charles Nesbitt, Ed Edmondson, and Dewey Bartlett.

12:00 p.m. **OSMA ANNUAL TENNIS TOURNAMENT.** The tournament will be held at the Will Rogers Memorial Tennis Center. Men's singles and doubles will be played with consolation rounds for the first round losers. A wives' tournament is also being planned with singles and doubles competition. Winners will be announced and trophies awarded at the President's Inaugural Dinner-Dance on Saturday evening. Send entry in advance to Farris W. Coggins, MD, 5700 N.W. Grand Blvd., Oklahoma City, Oklahoma 73112.

Friday Afternoon, May 19th

1:30 p.m. **CORONARY HEART DISEASE 1972.** Coronary Heart Disease, still the leading cause of death in our 20th century civilization, poses a major challenge to clinicians and researchers in virtually every field of medicine. A panel of four experts from the Mayo Clinic will conduct an in depth look into what we actually know about its causes, prevention, and treatment. They will cover such topics as the roll of monitoring, pacemakers, physical exercise, coronary arteriography and of surgery. Risk factors and the use of the stress test in diagnosis will be discussed. Moderator—Dale Groom, MD. Speakers—Robert O. Brandenberg, MD; Daniel C. Conolly, MD; Ralph E. Smith, MD; Jack L. Titus, MD, PhD; all of the Mayo Clinic, Rochester, Minnesota.

Friday Evening, May 19th

5:30 p.m. **POOLSIDE COCKTAIL PARTY.** A free cocktail party will be held from 5:30 p.m. until 7:00 p.m. around the Skirvin Hotel's Sun Suite Swimming Pool. All OSMA members and and their wives are invited to attend.

Saturday Morning, May 20th

8:30 a.m. **ANESTHESIOLOGY SECTION.** "A Concept of Shock and Some New Agents in its Treatment," "Clinical Pharmacology of Muscle Relaxants," "Recent Studies of Muscle Relaxants and Their Antagonists." Speaker—Ronald L. Katz, MD, New York City, New York.

8:30 a.m. **PATHOLOGY SECTION.** "Clinical Laboratory Parasitology," "Clinical Laboratory Study of Hemorrhagic Diatheses." Speaker—John H. Thompson, Jr., PhD, Mayo Clinic, Rochester, Minnesota.

8:30 a.m. **OTOLARYNGOLOGY SECTION.** "Symposium of Facial Trauma," "Fractures of the Nasal Pyramid"—Donald R. Resler, MD; "Fractures of the Frontal Bone"—John G. Campbell, MD; "Fractures of the Zygoma"—A. Munson Fuller, MD; "Occlusion and Occlusal Problems"—Kenneth A. Rogers, Jr., MD; "Fractures of the Mid-Face"—William Jack Preston, MD; "Fractures of the Mandible"—H. Craig Pitts, MD.

8:30 a.m. **INTERNAL MEDICINE SECTION.** Richard L. Wilbur, MD, former Deputy Executive Vice-President of the AMA and now an Undersecretary in the U.S. Department of Defense.

9:30 a.m. **HEALTH MAINTENANCE ORGANIZATIONS SYMPOSIUM.** Health Maintenance Organizations, a major plank in President Nixon's health program, represent a controversial departure from the traditional health care delivery system. Speakers from various levels of implementation will discuss the issue. Moderator—C. S. Lewis, Jr., MD. Speakers—W. L. Reimer, MD, Denver, Colorado; Gerald R. Riso, Department of Health, Education and Welfare, Rockville, Maryland; James Harvey, Hillcrest Hospital, Tulsa; James H. Sammons, MD, AMA Trustee, Baytown, Texas.

11:30 a.m. **FREE PICNIC LUNCHEON.** Pastrami and corned beef sandwiches, assorted side dishes and relishes, plus beer and soft drinks will be served in the Skirvin Hotel's Convention Center. Sponsored by the Insurance Company of North America.

Saturday Afternoon, May 20th

1:30 a.m. **ANESTHESIOLOGY SECTION.** Program continued from morning session.

1:30 p.m. **FUTURE OF MEDICINE SYMPOSIUM.** Medical practice is undergoing revolutionary changes that are being brought about not by scientific advancement but by economic and sociological pressures. The future of medicine is being dictated by sources outside of the profession, sources quite often completely unfamiliar with either the scientific or personal aspects of medicine. Four nationally recognized opinion leaders will discuss and predict medicine's future. Max Parrott, MD, is the knowledgeable and articulate Chairman of the AMA Board of Trustees. Richard L. Wilbur, MD, is former Deputy Executive Vice-President of the AMA and now an Undersecretary in the U.S. Department of Defense. Wilbur J. Cohen, PhD, is one of the foremost social planners of the day and a principle architect of Medicare. Jenkin Lloyd Jones is the Past-President of the U.S. Chamber of Commerce, Publisher of the Tulsa Tribune, and an internationally known syndicated columnist. Moderator—Rex Kenyon, MD.

Saturday Evening, May 20th

6:00 p.m. **PRESIDENT'S INAUGURAL DINNER-DANCE.** The social highlight of the year will begin with a 6:00 p.m. cocktail party followed by a banquet, inaugural ceremony, entertainment and dancing in the Skirvin Tower Hotel's beautiful Persian Room. A gourmet dinner will be served, entertainment will feature the Cry-Slurs and dancing will be to the music of the popular Al Good Orchestra.

ANNUAL MEETING

TELEPHONE MESSAGE CENTER

ATTENTION:

While you are attending the OSMA Annual Meeting in Oklahoma City, your emergency calls may be referred to:

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A courtesy message center will be maintained by Southwestern Bell Telephone during the 66th OSMA Annual Meeting in the Skirvin Hotel Convention Center.

Entertainment Schedule

HOUSE OF DELEGATES RECEPTION AND DINNER

5:00 p.m.—May 18th—Persian Room, Skirvin Tower Hotel

Members of the House of Delegates and other interested members of the OSMA are invited to a cocktail hour and dinner meeting on Thursday evening, prior to the closing session of the OSMA House of Delegates. Featured speaker for the meeting will be Max H. Parrott, MD, Portland, Oregon, Chairman of the American Medical Association's Board of Trustees. Dinner tickets are $5.00 each.

COCKTAILS ALFRESCO

5:30 p.m.—May 19th—Skirvin Hotel's Sun Suite Swimming Pool

Cocktails, conversation, and music will be the bill of fare for the poolside cocktail party from 5:30 until 7:00 p.m. on Friday evening. All members of the association and their guests are invited to attend. Music will be provided by strolling mariachies. A number of specialty societies have dinner meetings planned following the cocktail party.



Al Good

INAUGURAL DINNER - DANCE

6:00 p.m.—May 20th—Persian Room, Skirvin Tower Hotel

Beginning with a cocktail party at 6:00 p.m. and concluding with dancing until midnight, the President's Inaugural Dinner-Dance is the highlight of the OSMA annual social calendar. After cocktails, there is a gourmet banquet with wine service, the inauguration of Stanley R. McCampbell, MD, as OSMA President, entertainment by the nationally known Cry-Slurs of Northwest High School, and dancing to the popular Al Good Orchestra.



Cry-Slurs, Northwest High School

The menu for the banquet includes Coquille St. Jacques A La Mariniere, Tenderloin of beef demi glacè, fresh peas and potato croquettes A La Berney, Princess Salad, all of which will be complimented by an appropriate wine. Dessert for the evening will be Cherries Jubilee.

Tickets should be purchased in advance from the Oklahoma State Medical Association, $12.50 each.

Technical Exhibitors

The Technical Exhibits of the 66th Annual Meeting of the Oklahoma State Medical Association may be seen in the Skirvin Hotel Convention Center.

Ames Company

Astra Pharmaceutical Products, Inc.

Audio Equipment Company

Beecham-Massengill Pharmaceuticals

R. K. Black, Inc.

Ralph Bolen Imports, Ltd.

Bristol Laboratories

Casualty Indemnity Exchange

Ciba Pharmaceutical Company

Coca Cola USA

Jackie Cooper Leasing, Inc.

Encyclopaedia Britannica

Flint Laboratories

***Geigy Laboratories**

Horaney's Sporting Goods

Insurance Company of North America

Eli Lilly and Company

Medco Products Co., Inc.

Murray Myers Company

Nationwide Pension Planning Inc.

Niagara Cyclo-Massage of Oklahoma

Oklahoma Regional Medical Program

Organon Pharmaceuticals

Ortho Pharmaceuticals Corporation

OSMA Insurance Program

Physicians Planning Service

Richard's Manufacturing Company

***A. H. Robins Company**

William H. Rorer, Inc.

Sandoz Pharmaceuticals

G. D. Searle & Co.

Seven-Up Bottling Company of Oklahoma City, Inc.

E. R. Squibb & Sons, Inc.

Stuart Pharmaceuticals, Division of Atlas Chemical Ind., Inc.

The Upjohn Company

USV Pharmaceutical Corporation

*Contributor to Scientific Program

Scientific And Institutional Exhibitors

"Clinical Spirometry"—R. J. Dougherty, MD, Oklahoma City

"Surgery of Coronary Artery Disease"—Doctors Greer, Carey, Zuhdi and Halley, Oklahoma City

"Rehabilitative Office Procedures for the Aging Face"—D. B. Stough, III, MD, Hot Springs, Arkansas

"Surgery of Coronary Artery Disease"—Joseph M. St. Ville, MD, Tulsa, Oklahoma

American Cancer Society

National Drug Education Center

Oklahoma Pharmaceutical Association

Oklahoma Tuberculosis Association

AGENDA*

House of Delegates Meetings

ANNUAL MEETING—OPENING SESSION

8:30 a.m., May 18th, Skirvin Hotel Convention Center

I. Call to Order
II. Report of Credentials Committee
III. Introduction of Guests
IV. Remarks of Speaker
V. Nominations for Elections
VI. Report of President
VII. Board of Trustees' Report
VIII. Treasurer's Report
IX. Council, Committee Reports
X. Introduction of Resolutions
XI. Necrology Report

(Reference Committees will meet at 10:00 a.m., May 18th, 2nd Floor, Skirvin Hotel)

ANNUAL MEETING—CLOSING SESSION

7:30 p.m., May 18th, Skirvin Hotel Convention Center

I. Call to Order
II. Report of Credentials Committee
III. Reference Committee Reports
IV. Elections
V. Adjournment

*Condensed Version, Subject to Modification

OFFICERS TO BE ELECTED

President-Elect (One-Year Term)
Vice-President (One-Year Term)
Speaker of the House of Delegates (Two-Year Term)
Vice-Speaker of the House of Delegates (Two-Year Term)
Delegate to the AMA, Position I (Two-Year Term)
Alternate Delegate to the AMA, Position I (Two-Year Term)
Delegate to the AMA, Position II (Two-Year Term)
Alternate Delegate to the AMA, Position II (Two-Year Term)
Trustees From Districts XI through XIV

Oklahoma State Medical Association

1972 DELEGATES AND ALTERNATES

SOCIETY	DELEGATE	ALTERNATE DELEGATE
ALFALFA, WOODS	Ed L. Calhoon, MD	
ATOKA, BRYAN, COAL	Alfred T. Baker, MD	R. R Moose, MD
BECKHAM	William M. Leebron, MD	H. K Speed, MD
BLAINE	Not reported	
CADDO	A C. Roberson, MD	J. B. Miles, MD
CANADIAN	F W. Hollingsworth, MD	E. W. Young, Jr., MD
CARTER, LOVE,	Frank W. Clark, MD	Edward L. Koger, MD
MARSHALL	James Y. Miller, MD	Michael W. Brown, MD
CHOCTAW, PUSHMATAHA	Bill E. Woodruff, MD	Austin W Haddox, MD
CLEVELAND,	William C. McCurdy, MD	W. George Long, MD
McCLAIN	Edwin A. McGrew, MD	Fred Beckett, MD
	Hayden H Donahue, MD	James L. Haddock, MD
	James V. Simmering, MD	Robert R. Sullivan, MD
COMANCHE,	William A. Matthey, MD	Paul N. Vann, MD
COTTON	Robert R. Hillis, MD	Jack D. Honaker, MD
COOKSON HILLS	Kenneth L. Koehn, MD	Burdge F. Green, MD
CRAIG, DELAWARE, OTTAWA	Charles H Price, MD	Don H Olson, MD
CREEK	Oliver H. Patterson, MD	Merrill S. Bartlett, MD
CUSTER	Ross Deputy, MD	J. Harold Tisdal, MD
EAST CENTRAL	Tom S. Gafford, MD	Chester K. Mengel, MD
	Ann K. Kent, MD	Emil F. Stratton, MD
	Richard E. Witt, MD	Harvey P. Randall, MD
	Glen L. Berkenbile, MD	Port E. Johnson, MD
GARFIELD	Paul H Rempel, MD	Joseph W. Stafford, MD
	Avery B. Wight, MD	Joe B. Jarman, Jr., MD
	Robert D. Shuttee, MD	Frank L. Adelman, MD
GARVIN	John M. Moore, MD	M. E Robberson, MD
GRADY	B. C. Chatham, MD	Charles Gibson, MD
GREER, HARMON	David Fried, MD	Phillip N. Kingery, MD
HUGHES, SEMINOLE	Claud B. Knight, MD	Jack W. Parrish, MD
JACKSON	Malcolm Mollison, MD	George A. Aldridge, MD
	Cooper D. Ray, MD	Lowell N. Templer, MD
JEFFERSON	Harold Stout, MD	W A. Heflin, MD
KAY, NOBLE	E. C Yeary, MD	Vernon C. Merrifield, MD
	E. H. Arrendell, MD	William O. Ellifrit, MD
	D. E. Becker, MD	Robert Gibson, MD
KINGFISHER	Frank C. Lattimore, MD	Ray V. McIntyre, MD
KIOWA, WASHITA	M. Wilson Mahone, MD	Malcolm Bridwell, MD
LeFLORE, HASKELL	Robert Hampton, MD	R. L. Winters, MD
LINCOLN	Harold T. Baugh, MD	G. Conrad Markert, MD
LOGAN	Robert J Hogue, Jr., MD	Curtis O Bohlman, MD
McCURTAIN	Thomas Rhea, MD	Thomas D. Howard, MD
MURRAY	Luis R. Galainena, MD	Jack W. Donald, MD
NORTHWEST	Not reported	
OKFUSKEE	Thomas W. Coale, MD	Noel E. Miller, MD
OKLAHOMA	Martin H. Andrews, MD	D. D. Albers, MD
	Charles N. Atkins, MD	Charles D. Bodine, MD
	H. T. Avey, MD	Donald R. Carter, MD
	John A. Blaschke, MD	William O Coleman, MD
	Kent Braden, MD	Myron A. Cordum, MD
	Jerry L. Bressie, MD	Ernest R. Daffer, MD
	R. Barton Carl, MD	Charles E. Delhotal, MD
	R. Leroy Carpenter, MD	Ralph C. Denny, MD
	Charles W. Cathey, MD	J. B. Eskridge, III, MD
	John W. DeVore, MD	Mark A. Everett, MD
	John W. Drake, MD	James F. Hampton, MD

	J. Hartwell Dunn, MD	Thomas H. Henley, MD
	Arthur F. Elliott, MD	Elwood Herndon, MD
	Robert S. Ellis, MD	L. O. Laughlin, MD
	Lynn H. Harrison, MD	Irwin C. McLendon, MD
	William E. Hood, MD	Bertha M. Levy, MD
	David C. Lowry, MD	Robert A. McLauchlin, MD
	James E. Mays, MD	John F. Montroy, MD
	Robert J. Morgan, MD	Francis D. Oakes, MD
	James B. Pitts, Jr., MD	William L. Parry, MD
	Don F. Rhinehart, MD	C. Dowell Patterson, MD
	John W. Richardson, Jr., MD	William S. Pugsley, MD
	Orville L. Rickey, Jr., MD	John W. Records, MD
	Clarence Robison, Jr., MD	Donald R. Resler, MD
	Bobby G. Smith, MD	Edward A. Shadid, MD
	J. B. Snow, Jr., MD	Julian W. Swann, MD
	Armond H. Start, MD	Lal D. Threlkeld, MD
	W. David Stuart, MD	Stephen Tkach, MD
	Robert Sukman, MD	James B. Wise, MD
	Marion C. Wagnon, MD	C. Jack Young, MD
OKMULGEE	R. L. Alexander, Jr., MD	Jack Meyers, MD
OSAGE	Richard F. Harper, MD	John L. Hudson, MD
PAYNE, PAWNEE	George R. Smith, MD	Lanny F. Trotter, MD
	Taylor D. Wagner, MD	Clifford M. Bassett, MD
PITTSBURG	George M. Brown, MD	Thurmond Shuller, MD
	Joe W. McCauley, MD	William G. Blanchard, MD
PONTOTOC	Clarence P. Taylor, Jr., MD	J. B. Wallace, MD
	David C. Ramsay, MD	Carl D. Wiseman, MD
POTTAWATOMIE	Leon D. Combs, MD	William C. Click, MD
	Roy O. Kelly, Jr., MD	Jake Jones, Jr., MD
ROGERS, MAYES	Pat Williams, MD	Peter Sarfatis, MD
STEPHENS	C. H. Smith, MD	Charles N. Talley, MD
TEXAS, CIMARRON	J. C. Hallford, MD	
TULSA	Norman L. Dunitz, MD	John R. Alexander, MD
	Homer D. Hardy, Jr., MD	William D. Putnam, MD
	Robert A. Northrup, MD	Charles J. Bate, MD
	Duane E Brothers, MD	Craig S. Jones, MD
	Robert D. Grubb, MD	Roger M. Atwood, MD
	Emil E. Palik, MD	Norman L. Bartlett, MD
	James E. White, MD	John H. Smith, MD
	Byron W. Steele, MD	Walter H. Gary, MD
	Roger V. Haglund, MD	Victor L. Robards, Jr., MD
	Bernard E. Guenther, MD	Dale E. Van Wormer, MD
	Frank A. Clingan, MD	Edward W. Jenkins, MD
	Clayton E. Woodard, MD	James C. Smith, Jr., MD
	Jerry Sisler, MD	Harry E. Livingston, MD
	C. S. Lewis, Jr , MD	Fred R. Martin, MD
	Floyd F. Miller, MD	Bernard J. Maguire, MD
	Robert L. Imler, Jr., MD	Jack E. Hale, MD
	Lynwood Heaver, MD	Hugh Perry, Jr., MD
	Robert M. Shepard, Jr., MD	William G. Mays, MD
	Harold W. Calhoon, MD	Edward O. Nonweiler, MD
	Henry H. Modrak, MD	Robert S. White, MD
WASHINGTON,	Clair Liebrand, MD	J. W. Cochran, MD
NOWATA	Elvin M. Amen, MD	John E. Scott, MD
	John R. Reid, MD	Orville L. Grigsby, MD

WOMAN'S AUXILIARY

OKLAHOMA STATE MEDICAL ASSOCIATION

MAY 18th, 19th, 20th, 1972 **SKIRVIN HOTEL**

OKLAHOMA CITY, OKLAHOMA



MRS. E. COTTER MURRAY
Oklahoma City
President



MRS. PORT E. JOHNSON
Muskogee
President-Elect



MRS. G PRENTISS LEE
Portland, Oregon
President, Auxiliary to the American Medical Association



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Louisville, Kentucky
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MRS. JOHN W. WILLIAMS
Enid
1st Vice-President



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Shawnee
Treasurer-Elect



MRS. VIRGIL RAY FORESTER
Oklahoma City
Convention Chairman



MRS. CLINTON GALLAHER
Shawnee
Convention Co-Chairman



MRS. DAVID W. HAMBLIN
Oklahoma City
President, Woman's Auxiliary to the Student American Medical Association



MRS. F. M. GILHAUSEN
Oklahoma City
President, Interns and Residents Wives



MRS. KEN D. GERMAN
Oklahoma City
National Secretary to the Student American Medical Association



MRS. DAVID COWDEN
Oklahoma City
National Regional Co-ordinator, Woman's Auxiliary to the Student American Medical Association

GENERAL INFORMATION

REGISTRATION
Second Floor Lobby—Skirvin Hotel

Mrs. Robert J. Morgan, Chairman

Thursday, May 18th	1:00 p.m.-5:00 p.m.
Friday, May 19th	8:00 a.m.-5:00 p.m.
Saturday, May 20th	8:00 a.m.-12:00 Noon

MEDICAL ADVISORS

William M. Leebron, MD
Arnold G. Nelson, MD
C. Riley Strong, MD

HOSPITALITY ROOM

Second Floor Lobby—Skirvin Hotel
Executve Suite, Thursday and Friday

Mrs. Earl M. Bricker, Jr.

These rooms will be open during registration hours Thursday and Friday for the convenience of guests. Refreshments will be available, including a Continental breakfast Friday.

CONVENTION COMMITTEE

CHAIRMAN: Mrs. Virgil Ray Forester

CO-CHAIRMAN: Mrs. Clinton Gallaher

Courtesy	Mrs. W. Tom Buxton
Credentials	Mrs. J. Hartwell Dunn
Decorations and Luncheon	Mrs. Virgil Ray Forester, Mrs. Clinton Gallaher and Mrs. E. Cotter Murray
Luncheon Properties	Mrs. William Best Thompson
Hospitality	Mrs. Earl M. Bricker
Timekeeper	Mrs. Thermon McInnis
Pages	Mrs. Ronald H. White, Mrs. Daniel R. Stough
Publicity	Mrs. Daniel R. Stough
Registration	Mrs. Robert J. Morgan
Past-Presidents' Breakfast	Mrs. Tom C. Sparks
Style Show	Mrs. Richard A. Clay, Mrs. David I. Kraft
Tickets	Mrs. P. D. Casper

Tickets for Past-Presidents' Breakfast, Luncheon and Style Show, and the Workshop Breakfast will be on sale at the Registration Desk in the Second Floor Lobby

PROGRAM

THURSDAY, MAY 18th, 1972

1:00 p.m.-5:00 p.m. — REGISTRATION AND HOSPITALITY
Second Floor Lobby—Skirvin Hotel

2:00-4:00 p.m. — PRE-CONVENTION BOARD MEETING, Home of Doctor and Mrs. Virgil Ray Forester, 2336 Belleview Drive, Oklahoma City

FRIDAY, MAY 19th, 1972

8:00 a.m.—PAST-PRESIDENTS' BREAKFAST
By pool in Sun Suite, Skirvin Hotel, Mrs. Tom C. Sparks, Chairman

8:00 a.m.-5:00 p.m. — REGISTRATION AND HOSPITALITY, Second Floor Lobby, Skirvin Hotel

9:00 a.m.—FIRST GENERAL SESSION, Venetian Room, Fourteenth Floor, Skirvin Hotel, Mrs. E. Cotter Murray, President, Woman's Auxiliary to the Oklahoma State Medical Association, presiding

CALL TO ORDER: Mrs. E. Cotter Murray

PLEDGE OF ALLEGIANCE TO FLAG: Mrs. Jack W. Newport

MUSIC: Mrs. Raymond E. Peeples

INVOCATION: Mrs. George H. Miller

PLEDGE OF LOYALTY: Mrs. Stanley R. McCampbell, wife of the President-Elect of the Oklahoma State Medical Association

WELCOME: Mrs. Neil B. Kimerer

RESPONSE: Mrs. Michael W. Brown

ANNOUNCEMENTS: Mrs. Virgil Ray Forester

GREETINGS: Lucien Pascucci, MD, President, Oklahoma State Medical Association

INTRODUCTION OF SPECIAL GUESTS: Mrs. G. Prentiss Lee, Portland, Oregon, President, Woman's Auxiliary to the American Medical Association; Mrs. Raymond E. Jones, Louisville, Kentucky, President, Woman's Auxiliary to the Southern Medical Association

ROLL CALL BY COUNTIES: Mrs. Bryce Petrie, Secretary

REPORT OF CREDENTIALS COMMITTEE: READING OF MINUTES. Mrs. Bryce Petrie, Secretary

TREASURER'S REPORT: Mrs. Leonard W. Rozin

GUEST SPEAKER: Mrs. Raymond E. Jones, Louisville Kentucky, President, Woman's Auxiliary to the Southern Medical Association

REPORTS OF OFFICERS. (Two minute reports)
President: Mrs. E. Cotter Murray
President-Elect: Mrs. Port E. Johnson
First Vice-President: Mrs. John W. Williams
Second Vice-President: Mrs. Daniel R. Storts
Editor of *Sooner Physician's Wife*: Mrs. Richard E. Witt
Editor of Auxiliary Page in *The Journal*: Mrs. James B. Silman

Report of Nominating Committee: Mrs. Port E. Johnson, President-Elect

ELECTION OF OFFICERS

12:00 noon—LUNCHEON AND STYLE SHOW, Persian Room, Skirvin Tower

INSTALLATION OF OFFICERS: Mrs. G. Prentiss Lee, President, Woman's Auxiliary to the American Medical Association

INAUGURAL ADDRESS: Mrs. Port E. Johnson, President, Woman's Auxiliary to the Oklahoma State Medical Association

SPEAKER: Mrs. G. Prentiss Lee

ETRAVAGANZA—Honoring Fiftieth Anniversary of the Woman's Auxiliary to the American Medical Association and the Sixty-fifth Anniversary of the Woman's Auxiliary to the Oklahoma State Medical Association
STYLE SHOW: Fashions by Balliets with commentary by Althea Notson

2:30 p.m.—SECOND GENERAL SESSION—Venetian Room, Fourteenth Floor, Skirvin Hotel

ANNOUNCEMENTS: Mrs. Clinton Gallaher

REPORTS OF COMPONENT AUXILIARY PRESIDENTS:

Atoka-Bryan-Coal	Mrs. Alfred T. Baker
Carter-Love-Marshall	Mrs. Michael W. Brown
Cleveland-McClain	Mrs. J. Robert Dille
Comanche-Cotton	Mrs. Ronald E. Cagle
Custer	Mrs. Douglas D. Leatherman
East Central	Mrs. Harvey P. Randall
Garfield	Mrs. Joe B. Jarman, Jr.
Grady-Caddo	Mrs. Rugie R. Coates
Kay-Noble	Mrs. Robert F. Morgan
Oklahoma	Mrs. Neil B. Kimerer
Okmulgee	Mrs. Arthur L. Buell
Pittsburg	Mrs. Delta W. Bridges, Jr.
Pontotoc-Johnston	Mrs. Gordon H. Deen
Pottawatomie	Mrs. James D. Loudon
Stephens	Mrs. John L. Bond
Tulsa	Mrs. Jack W. Newport
Washington-Nowata	Mrs. James S. Williams

WASAMA: Mrs.David W. Hamblin
INTERNS AND RESIDENTS WIVES: Mrs. F. M. Gilhousen

UNFINISHED BUSINESS

NEW BUSINESS

ELECTION OF DELEGATES TO NATIONAL CONVENTION

PRESENTATION OF PRESIDENT'S GAVEL AND PIN: Mrs. E. Cotter Murray

PRESENTATION OF PAST-PRESIDENT'S EMBLEM: Mrs. William M. Leebron

MEMORIAL SERVICE: Mrs. Clifford M. Bassett
COURTESY RESOLUTIONS

SATURDAY, MAY 20th, 1972

8:30 a.m.—POST-CONVENTION WORKSHOP BREAKFAST

9:00 a.m. — POST-CONVENTION WORKSHOP, Continental Room, 14th Floor, Skirvin Hotel
Outgoing Board Members, Councilors, Component Auxiliary Presidents, Past State Presidents, and any auxiliary member wishing to attend. Members-At-Large are urged to attend.

1:30 p.m. Room A, Skirvin Hotel—Panel—Future of American Medicine, Rex E. Kenyon, MD, Moderator

2:30 p.m. — MEMBERS-AT-LARGE TEA, President's Suite, Skirvin Hotel

6:00 p.m.—SOCIAL HOUR, Persian Room, Skirvin Hotel

7:00 p.m. — PRESIDENT'S INAUGURAL DINNER-DANCE, Persian Room, Skirvin Hotel

ANNUAL MEETING

TELEPHONE MESSAGE CENTER

ATTENTION:

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Miscellaneous Advertisements

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SURGEON LOOKING FOR LOCATION. Graduate of Paris Medical School; U.S. internship and residency; licensed in New York and Pennsylvania. Board eligible. Contact A. Sergie, MD, 113 Duncan Street, Dublin, Georgia 31021.

MEDICAL CLINIC. Space for two doctors, dentist already in building. Plenty of parking space. C. A. Walker, 946-5157, 946-1942, 427-8631. W. A. Hutchison, 943-1763, Oklahoma City.

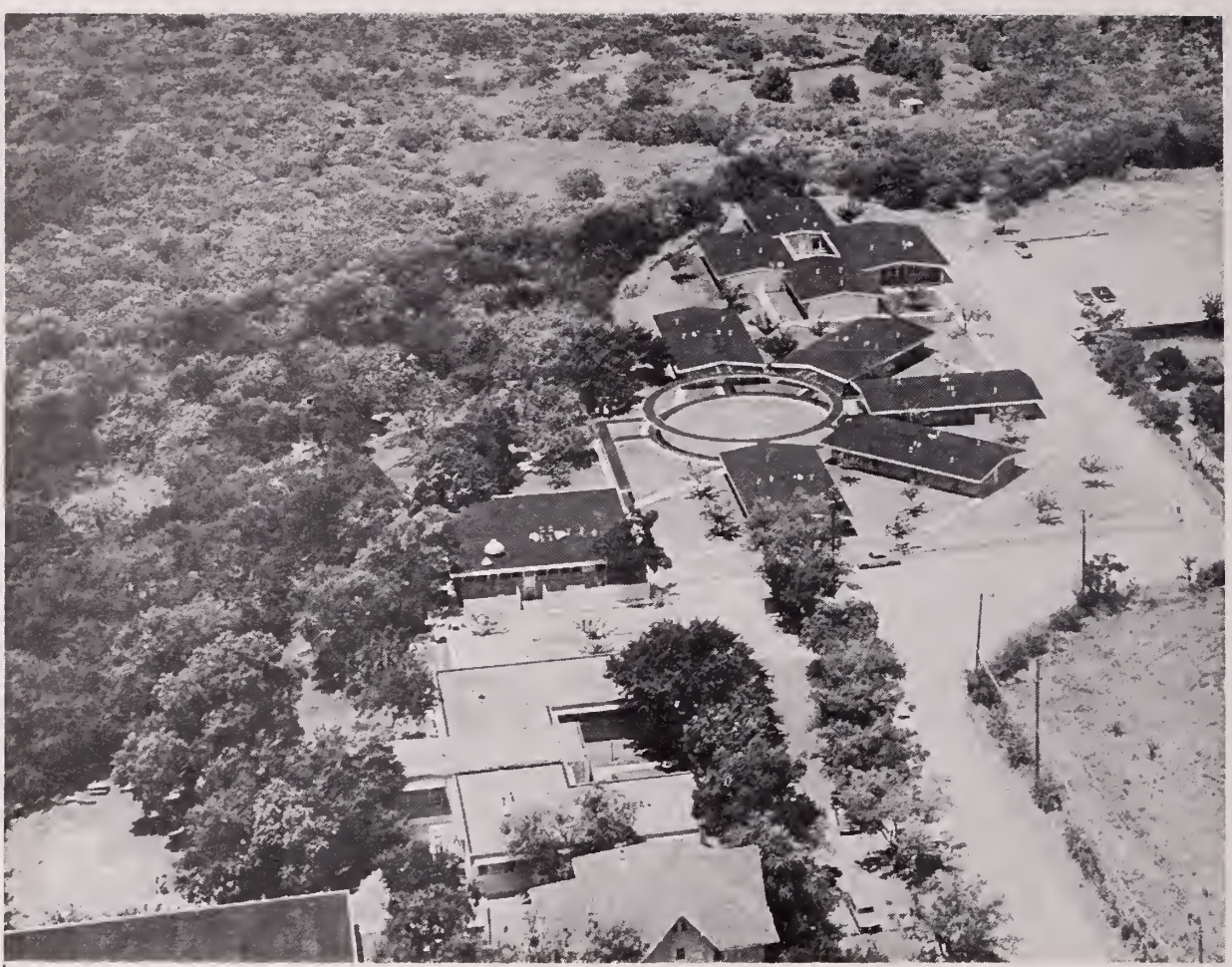
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OPPORTUNITY FOR GENERAL PRACTICE (with specialty interest if desired) in El Reno, a city of 15,000 only thirty minutes west of Oklahoma City. Established clinic of three doctors, adjacent to modern community hospital desires one or two associates for active group practice. Attractive salary and partnership opportunity. Let us show you a good deal. Contact Canadian Valley Clinic, 2001 Park View, El Reno, Oklahoma 73036 or call collect 405 262-2114, F. W. Hollingsworth, MD.

FOR RENT because of leaving town. Excellent office space by Baptist Hospital—1,385 square feet—more space for less rent. Large waiting room, doctor's office, business office, secretary office and working area, storage, laboratory room, four examining rooms, and x-ray and dark room in The Clinic Building, 3434 N.W. 56th Street. Three year sub-lease by William L. Waldrop, MD. Also for sale: 200 Milliamperes General Electric Patrician in perfect working order. Complete accessories, complete dark room equipment, and film dryer. Cheap price, because it is mostly tax depreciated.

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HISTORIC EPHESUS

One of the exciting places to visit on the upcoming Mediteranean Adventure Air/Sea Cruise is Ephesus, reached through the port city of Izmir.

140/90 is normal blood pressure...or is it?

An extensive study based on nearly 4 million life insurance policies suggests that a blood pressure reading of 140/90 requires close medical supervision.

Study Findings. Twelve years ago the Society of Actuaries reported on an extensive study based on the lives and deaths represented by almost 4 million life insurance policies. From this vast survey—"The Build and Blood Pressure Study"[1]—insurance experts concluded that:

- Blood pressure above 140/90 is accompanied by increased morbidity and requires close medical attention.
- Even small increments in either systolic or diastolic blood pressure progressively and steeply shorten life expectancy.

Other Studies. Studies conducted with large numbers of patients since that time have echoed the above findings. Two studies published in 1970—the VA Cooperative Study Group on "Effects of Treatment on Morbidity in Hypertension"[2] and the "Framingham Study"[3]—suggest that treatment of even mild hypertension may, over time, offer significant benefits to the patient.

Another Point of View. Although a growing body of studies suggests that treatment of mild hypertension is warranted, medical opinion is not unanimous. Some clinicians recommend that drug treatment for mild hypertension be reserved for patients with additional risk factors such as smoking, high cholesterol levels, heart or kidney involvement, or a family history of vascular disease. Dr. Walter M. Kirkendall stated this position in his recent paper "What's With Hypertension These Days?"[4] Discussing the management of hypertension in patients with a sustained diastolic pressure up to 100 mm Hg, he said: "Generally, I do not recommend antihypertensive therapy unless patient's blood pressure approaches the upper limit for the group and a number of adverse factors exist, such as male sex, family history of vascular disease, youth, evidence of heart or kidney involvement."



Drug Therapy for Hypertension. Although opinion varies on when to start drug therapy for mild hypertension, many physicians agree that treatment should start with a thiazide diuretic such as HydroDIURIL. For the adult patient, the usual starting dosage is 50 mg b.i.d. Dosage adjustments are recommended as the patient responds to treatment. The patient whose therapy begins with HydroDIURIL frequently can continue to benefit from it, because HydroDIURIL usually maintains its antihypertensive effect even when therapy is prolonged.

MSD
MERCK SHARP & DOHME

25- and 50-mg tablets

HydroDIURIL®

(Hydrochlorothiazide|MSD)

Therapy to Start With

For a brief summary of prescribing information, please see next page.

1. Society of Actuaries, *The Build and Blood Pressure Study*, 1959.
2. Veterans Administration Cooperative Study Group on Antihypertensive Agents, "Effects of Treatment on Morbidity in Hypertension," JAMA *213*:1143-1152, Aug. 17, 1970.
3. Kannel, William B., *et al.*: "Epidemiologic Assessment of the Role of Blood Pressure in Stroke—The Framingham Study," JAMA *214*:301-310, Oct. 12, 1970.
4. Kirkendall, Walter M.: "What's With Hypertension These Days?" Consultant, Jan. 1971.

25- and 50-mg tablets

HydroDIURIL®

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Drug Therapy for Hypertension. Although opinion varies on when to start drug therapy for mild hypertension, many physicians agree that treatment should start with a thiazide diuretic such as HydroDIURIL. For the adult patient, the usual starting dosage is 50 mg b.i.d. Dosage adjustments are recommended as the patient responds to treatment. The patient whose therapy begins with HydroDIURIL frequently can continue to benefit from it, because HydroDIURIL usually maintains its antihypertensive effect even when therapy is prolonged.

CONTRAINDICATIONS: Anuria; increasing azotemia and oliguria during treatment of severe progressive renal disease. Known sensitivity to this compound. Nursing mothers; if use of drug is deemed essential, patient should stop nursing.

WARNINGS: May precipitate or increase azotemia. Use special caution in impaired renal function to avoid cumulative or toxic effects. Minor alterations of fluid and electrolyte balance may precipitate coma in hepatic cirrhosis.

When used with other antihypertensive drugs, careful observation for changes in blood pressure must be made, especially during initial therapy. Dosage of other antihypertensive agents, especially ganglion blockers, must be reduced by at least 50% because HydroDIURIL potentiates their action.

Stenosis and ulceration of the small bowel causing obstruction, hemorrhage, and perforation have been reported with the use of enteric-coated potassium tablets, either alone or with nonenteric-coated thiazides. Surgery was frequently required, and deaths have occurred. Such formulations should be used only when indicated and when dietary supplementation is impractical. Discontinue immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occurs.

Thiazides cross placenta and appear in cord blood. In women of childbearing age, potential benefits must be weighed against possible hazards to fetus, such as fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

The possibility of sensitivity reactions should be considered in patients with a history of allergy or bronchial asthma. The possibility of exacerbation or activation of systemic lupus erythematosus has been reported for sulfonamide derivatives, including thiazides.

PRECAUTIONS: Check for signs of fluid and electrolyte imbalance, particularly if vomiting is excessive or patient is receiving parenteral fluids. Warning signs, irrespective of cause, are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances. Hypokalemia may develop (especially with brisk diuresis) in severe cirrhosis; with concomitant steroid or ACTH therapy; or with inadequate electrolyte intake. Digitalis therapy may exaggerate metabolic effects of hypokalemia, especially with reference to myocardial activity. Hypokalemia may be avoided or treated by use of potassium chloride or giving foods with a high potassium content. Similarly, any chloride deficit may be corrected by use of ammonium chloride (except in patients with hepatic disease) and largely prevented by a near normal salt intake. Hypochloremic alkalosis occurs infrequently and is rarely severe. In severely edematous patients with congestive failure or renal disease, a low salt syndrome may occur if dietary salt is unduly restricted, especially during hot weather.

Thiazides may increase responsiveness to tubocurarine. The antihypertensive effect of the drug may be enhanced in the postsympathectomy patient. Arterial responsiveness to norepinephrine is decreased, necessitating care in surgical patients. Discontinue drug 48 hours before elective surgery. Orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics.

Pathological changes in the parathyroid glands with hypercalcemia and hypophosphatemia have been seen in a few patients on prolonged thiazide therapy. The effect of discontinuing thiazide therapy on serum calcium and phosphorus levels may be helpful in assessing the need for parathyroid surgery in such patients. Parathyroidectomy has elicited subjective clinical improvement in most patients, but has no effect on hypertension. Thiazide therapy may be resumed after surgery.

Use cautiously in hyperuricemic or gouty patients; gout may be precipitated. May affect insulin requirements in diabetics; may induce hyperglycemia and glycosuria in latent diabetics.

ADVERSE REACTIONS: Rare reactions include thrombocytopenia, leukopenia, agranulocytosis, aplastic anemia, cholestasis, and pericholangiolitic hepatitis. Nausea, vomiting, diarrhea, dizziness, vertigo, paresthesias, transient blurred vision, sialadenitis, purpura, rash, urticaria, photosensitivity, or other hypersensitivity reactions may occur. Cutaneous vasculitis precipitated by thiazide diuretics has been reported in elderly patients on repeated and continuing exposure to several drugs. Scattered reports have linked thiazides to pancreatitis, xanthopsia, neonatal thrombocytopenia, and neonatal jaundice. When adverse reactions are moderate or severe, the dosage of thiazides should be reduced or therapy withdrawn.

For more detailed information, consult your MSD Representative or see the Direction Circular. Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa. 19486

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Current G.U. Research

Gantanol® in animals
sulfamethoxazole)



ontrol



12.5 mg sulfamethoxazole/kg of body weight



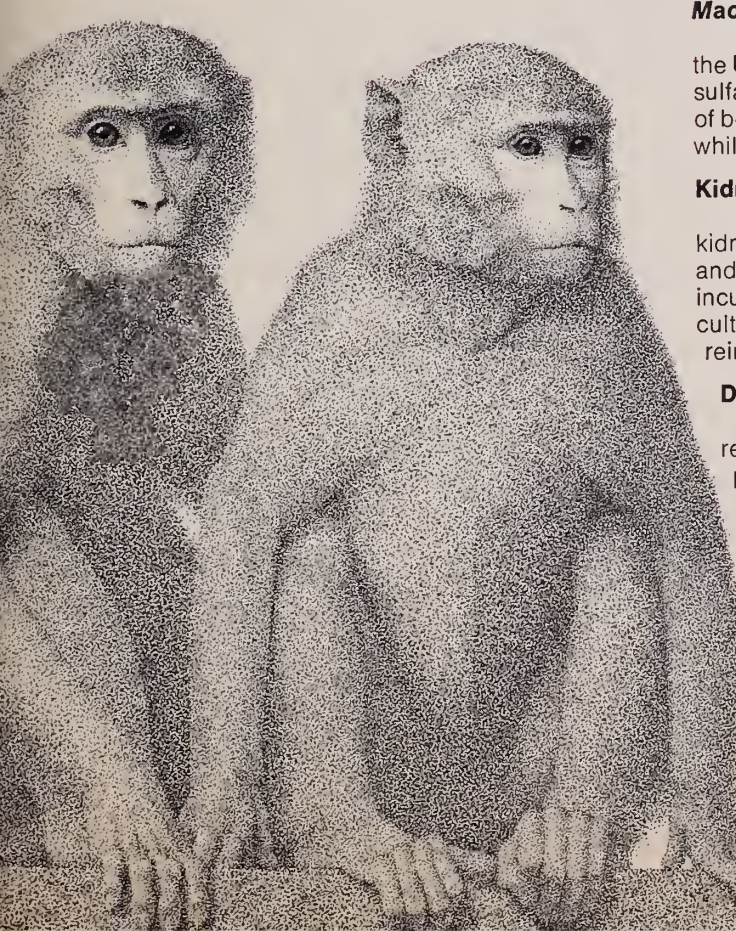
50 mg of sulfamethoxazole/kg of body weight



100 mg of sulfamethoxazole/kg of body weight

Tissue slice technique maps renal distribution in animal studies

Please note that while the method described may add to the knowledge of how antibacterial agents are distributed in the kidney of this animal, no conclusions can be drawn from this study relative to the drug's distribution, effect or use in humans, as it is not possible to extrapolate animal data to humans.



Gantanol® (sulfamethoxazole) administered to *Macaca speciosa* monkeys

Working with *Macaca speciosa* monkeys, researchers at the University of Arkansas Medical Center administered sulfamethoxazole at doses of 12.5 mg, 50 mg and 100 mg/kg of body weight. Each dosage level was given to three animals while three were left untreated as controls.*

Kidneys inoculated with *Staphylococcus aureus*

After 2½ hours, the 12 monkeys were sacrificed and their kidneys frozen with CO_2. Sagittal tissue slices were prepared and placed on blood agar bacteriological plates. They were incubated at 37°C. for 1½ hours. *Staphylococcus aureus* broth culture was then used to inoculate the tissue and slices were reincubated.*

Dark staining reveals heavy bacterial growth

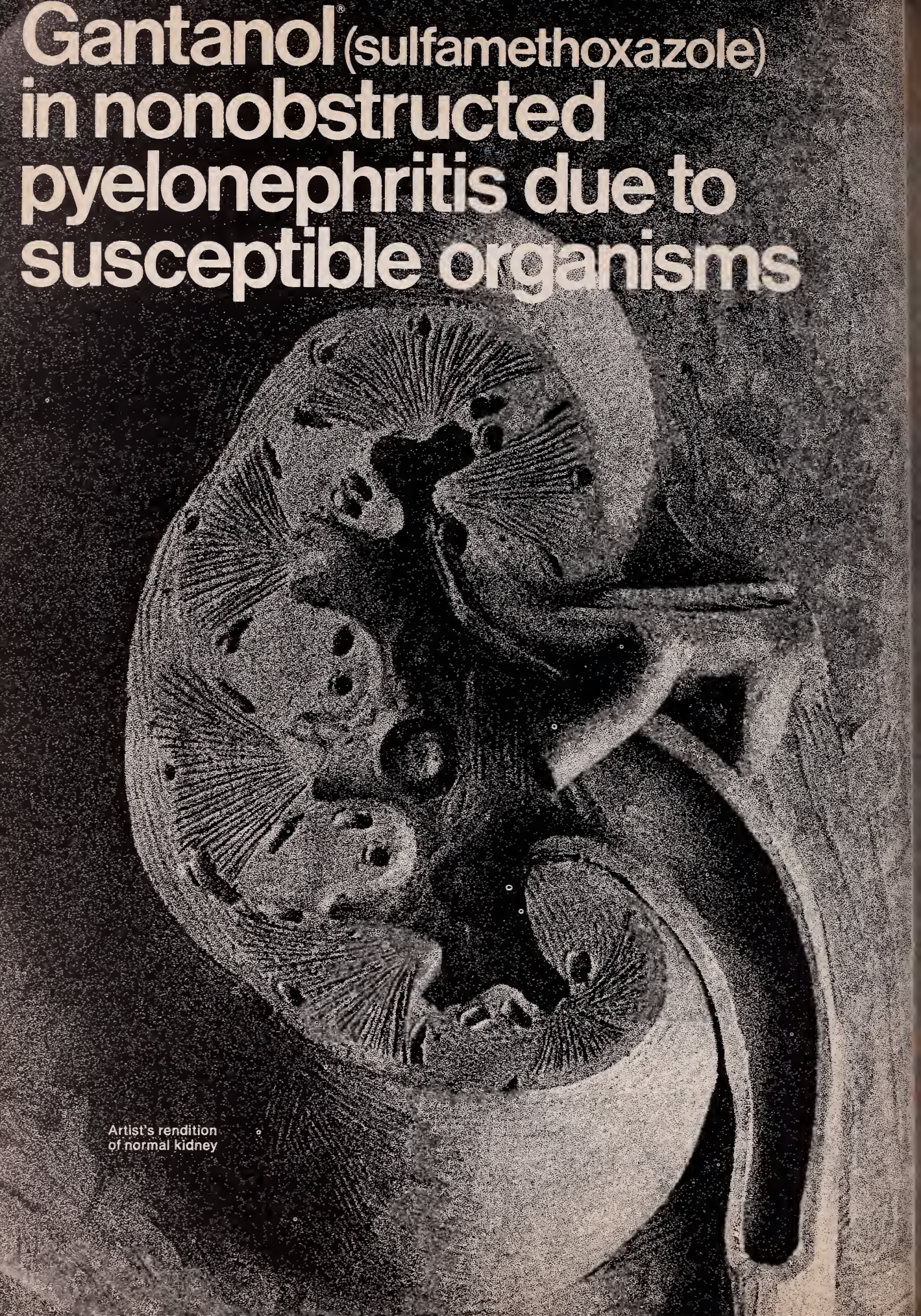
A solution of triphenyltetrazolium chloride, which turns a reddish purple in the presence of bacteria, was added to the plates after 6 hours. Renal slices from the untreated control animals consistently demonstrated heavy bacterial growth, as evidenced by dark staining.*

Distribution throughout *Macaca speciosa* renal parenchyma

At the dosage of 12.5 mg/kg of body weight, a diffuse stain pattern indicated partial inhibition of bacterial growth. Renal slices from monkeys given the 50 and 100 mg/kg doses showed no staining, indicating complete bacterial inhibition and *suggesting* antibacterial distribution throughout the parenchyma.*

*Mobley, J. E.; Redman, J. F., and Robbins, R. P.: *Surg. Gynec. Obstet.*, *131*:1122, 1970.

Gantanol® (sulfamethoxazole) in nonobstructed pyelonephritis due to susceptible organisms



Artist's rendition of normal kidney

Establishes antibacterial levels in blood and urine in from 2 to 3 hours

In from 2 to 3 hours of the initial 2-Gm adult dose, effective antibacterial levels of Gantanol® (sulfamethoxazole) are achieved in both blood and urine. This prompt, early treatment in acute nonobstructed pyelonephritis may help avert possible chronic sequelae.

Controls primary bacterial offenders

Antibacterial Gantanol (sulfamethoxazole) controls susceptible *E. coli*, the most common cause of urinary tract infections. It is also effective against other susceptible gram-negative and gram-positive urinary pathogens such as *Klebsiella-Aerobacter, Staph. aureus* and *Proteus mirabilis*.

Also effective in nonobstructed chronic and recurrent urinary tract infections

It is also common for the elderly and debilitated to develop chronic nonobstructed urinary tract infections, primarily pyelonephritis and cystitis. Such cases often respond satisfactorily to therapy with Gantanol.

B.I.D./T.I.D. schedule gives round-the-clock coverage

Subsequent 1-Gm doses can provide up to 12 hours of antibacterial activity. The *b.i.d.* dosage is recommended for mild to moderate infections; the *t.i.d.* for the more severe u.t.i. Gantanol provides coverage around the clock—coverage that is especially important during the hours of sleep, when urinary retention favors bacterial proliferation.

Your option: tablets or suspension

Gantanol is available in two convenient dosage forms—tablets or a pleasant-tasting suspension. It is generally well tolerated with relative freedom from complications. The usual precautions with sulfonamide therapy should be observed, including adequate fluid intake, frequent c.b.c.'s and urinalyses with microscopic examination. The most common side effects reported are nausea, vomiting and diarrhea. (It should also be noted that the increasing frequency of resistant organisms is a limitation of usefulness of antibacterial agents, including sulfonamides, especially in chronic or recurrent u.t.i.)

in nonobstructed pyelonephritis due to susceptible organisms

Gantanol®
(sulfamethoxazole)

Basic therapy

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Effective in acute, recurrent or chronic urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli, Klebsiella-Aerobacter, Staphylococcus aureus, Proteus mirabilis,* and, less frequently, *Proteus vulgaris*) and in the absence of obstructive uropathy or foreign bodies.

***Note:* Since *in vitro* sulfonamide sensitivity tests are not always reliable, carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response. Add aminobenzoic acid to culture media of patients receiving sulfonamides. The increasing frequency of resistant organisms is a limitation of usefulness of antibacterial agents, including sulfonamides, especially in chronic or recurrent urinary tract infections.**

Blood levels should be measured in patients receiving sulfonamides for serious infections, since there may be wide variations with identical doses; 20 mg/100 ml should be the maximum total sulfonamide level, as adverse reactions occur more frequently above this level.

Contraindications: Sulfonamide hypersensitivity; infants less than 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis); pregnancy at term and during nursing period.

Warnings: Safe use in pregnancy has not been established, and teratogenicity potential has not been thoroughly investigated. Sulfonamides will not eradicate or prevent sequelae to group A streptococcal infections, *i.e.,* rheumatic fever, glomerulonephritis. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported; early clinical signs such as sore throat, fever, pallor, purpura or jaundice may indicate serious blood disorders. Complete blood counts and urinalysis with careful microscopic examination are recommended frequently during sulfonamide therapy. Clinical data are insufficient on prolonged or recurrent therapy in chronic renal diseases of children under 6 years.

Precautions: Use with caution in patients with impaired renal or hepatic function, severe allergy, bronchial asthma and in glucose-6-phosphate dehydrogenase-deficient individuals. In the latter, dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias:* agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia; *allergic reactions:* erythema multiforme (Stevens-Johnson syndrome), skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis; *gastrointestinal reactions:* nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis; *C.N.S. reactions:* headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia; and *miscellaneous reactions:* drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide and thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age, except adjunctively with pyrimethamine in congenital toxoplasmosis. Usual dosage is as follows: *Adults*—2 Gm (4 tabs or teasp.) initially, then 1 Gm (2 tabs or teasp.) *b.i.d.* or *t.i.d.* depending on severity of infection. *Children*—0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially, followed by 0.25 Gm/20 lbs (½ tab or teasp.) *b.i.d.* Maximum dose for children should not exceed 75 mg/kg/24 hrs.

Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.

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—George Sarton, from "The History of Medicine Versus the History of Art"

Should nongovernment scientists and physicians play a role in drug regulation?

Opinion

Results of a questionnaire to 7000 physicians:

82.8%
Physicians should play a role

78.3%
Independent scientists should play a role

69.8%
Medical academicians should play a role

Opinion & Dialogue

Dialog

Should nongovernment scientists and physicians play a role in drug regulation?

Doctor of Medicine

Herbert L. Ley, Jr., M.D., M.P.H., Formerly Commissioner, F.D.A. (1968-1969)
Currently Medical Consultant

In order for drug regulation to be effective, participation in the regulatory process from nongovernment physicians and scientists must be encouraged. Without such involvement, there will continue to be a high degree of controversy surrounding any regulations promulgated by the Food and Drug Administration.

There are two areas in which participation and communication by nongovernment physicians and scientists could significantly improve the process of regulation. First, scientists and physicians throughout the country could become involved in consulting relationships with the Food and Drug Administration in important scientific areas while regulatory policies are being evolved. If nongovernment professionals could bring their expertise and experience to bear early in the decision-making process, they would have less reason to criticize the final outcome.

Secondly, practicing physicians, academic physicians, and academic-based scientists could make it their business to comment on proposed regulations appearing in the Federal Register. Ideally, a system could be instituted whereby medical, scientific and technical people could see the Federal Register regularly, and provide the Food and Drug Administration with a body of opinion that has so far gone unheard. The FDA is caught among pressures from industry, Congress, the Presidential Administration and consumers. It should also feel pressures from practicing physicians and scientists.

In order to become more involved in these stages of the drug regulatory process, nongovernment physicians and scientists should begin to exercise their influence through their respective professional organizations,



state and national medical societies, and specialty groups. Logically, a letter from these organizations representing a collective opinion has far greater weight in the regulatory process than individual letters. If the Food and Drug Administration receives opinions from these organizations early, before a regulation gets into the Federal Register, they are in a good position to respond with further study and review. Without such dissenting opinions, there is very little incentive to make changes in proposed regulations.

One instance in which practitioners did influence drug regulatory affairs in this way is the recent controversy that arose over the legitimacy of drug combinations. The strong opinion of practitioners on the value of such medication in clinical practice played a very prominent role in making the Food and Drug Administration modify its rather restrictive policy.

Another way in which practitioners can effectively influence drug regulations is by working with drug manufacturers conducting clinical trials of chemotherapeutic agents. When a drug is rated other than effective it may only mean that there is a lack of controlled clinical evidence as to efficacy. Thus, physicians might offer to conduct clinical studies that could help keep a truly effective drug in the marketplace. The treatment of diseases such as diabetes and angina are areas where the practitioner can aid in clinical studies because patients suffering from these diseases are rarely found in the conventional hospital setting.

By working with ethically and scientifically sound study designs in his everyday practice, the practitioner could begin to play an important part in determining official ratings on drug efficacy.

Nongovernment physicians and scientists and the FDA should also improve their lines of communication to the public. The medical community must develop a voice every bit as loud as that of the consumerists, the press, and others who sometimes criticize without complete information. If not, much of what the medical community *and* federal regulators do will often be represented in simplistic and somewhat misleading terms.

One illustration of the misuse of the media in this regard is the recall of anticoagulant drugs several years ago. This FDA action was given publicity by the press and television that went far beyond its probable importance. The result was a very uncomfortable situation for the practitioner who had patients taking these medications. Since the practitioner and pharmacist had not been informed of the action by the time it was publicized, in most states they were deluged with calls from worried patients.

The practitioner can attempt to solve these problems of inadequate communication in several ways. One would be the creation of a communications line in state pharmacy societies. When drug regulation news is to be announced, the society could immediately distribute a message to every pharmacist in the state. The pharmacist, in turn, could notify the physicians in his local community so that he and the physician could be prepared to answer inquiries from patients. Another approach would be to use professional publications the practitioner receives.

All of this leads back to my opening contention: if drug regulation is to be effective, timely, and related to the realities of clinical practice, a better method of communication and feedback must be developed between the nongovernmental medical and scientific communities and the regulatory agency.

ue

Maker of Medicine

Henry W. Gadsden, Chairman & Chief Executive Officer, Merck & Co., Inc.



In my opinion, it is the responsibility of all physicians and medical scientists to take whatever steps they think are desirable in a law- and regulation-making process that can have far-reaching impact on the practice of medicine. Yet many events in the recent past indicate that this is not happening. For example, it is apparent from drug efficacy studies that the NAS/NRC panels gave little consideration to the evidence that could have been provided by practicing physicians.

There are several current developments that should increase the concern of practicing physicians about drug regulatory affairs. One is the proliferation of malpractice claims and litigation. Another is the effort by government to establish the relative efficacy of drugs. This implies that if a physician prescribes a drug other than the "established" drug of choice, he may be accused of practicing something less than first-class medicine. It would come perilously close to federal direction of how medicine should be practiced.

In order to minimize this kind of arbitrary federal action, a way must be found to give practitioners both voice and representation in government affairs. Government must be caused to recognize the essentiality of seeking their views. One of the difficulties today, however, is that there is no way for concerned practitioners to participate in the early stages of decision-making processes. They usually don't hear about regulations until a proposal appears in the Federal Register, if then. By that time a lot of concrete has been poured, and a lot of boots are in the concrete.

Physicians in private practice, and particularly clinicians, should press for representation on the advisory committees of the Food and Drug Administration, joining with academic and teaching hospital physicians and scientists who are already serving. Though practitioners may not have access to all available information, the value of their clinical experience should be recognized. Clinicians, for example, rightly remind us that difficulty in *proving* precise effects does not necessarily mean a drug is ineffective.

Unless practitioners are more involved in drug regulations, it will be increasingly difficult for the pharmaceutical industry and scientists elsewhere to make optimal progress in drug development. The benefit/risk ratio must be re-emphasized, and as part of this it must be acknowledged that benefit can come from the judgments of medical science as a whole. Even this concept, unfortunately, is not always accepted in drug regulatory processes. For example, if current medical opinion holds that an excess of total lipids and cholesterol in the blood is probably predisposing to atherosclerosis, and if a drug is discovered which reduces total lipids and cholesterol, the drug ought to be accepted *prima facie* as a contribution to medical science . . . until someone disproves the theory. The sponsor should not have to prove the theory as well as to develop and test the drug.

I feel a major new effort must also be made to erase the feeling of mistrust of medicine and of medicines that seems to be growing in the public consciousness. Triggered primarily by strident announcements in Washington, people are reading and hearing confidence-shaking things almost continuously. Although challenge and awareness are essential to medical advancement, our long-term goal is constructively to build, not destroy. This means strengthening patient-physician relationships based on mutual confidence and trust. And in matters of health policy, it means working toward participatory rather than adversary proceedings—where everyone with an interest and a capacity to contribute has an opportunity to be heard . . . and, if that opportunity is not spontaneously afforded him, he may seek it.

Opinion & Dialogue

What is your opinion, doctor?
We would welcome your comments.

P·M·A

The Pharmaceutical Manufacturers Association
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Thank You, Doctor



Your continuing cooperation with the American Association of Medical Assistants has been generous. With your support our organization has achieved a membership of 14,000 medical assistants in more than 400 chapters in 45 states, District of Columbia and Puerto Rico.

Since our first organizational meeting 15 years ago, we have worked toward the primary goal of providing educational opportunities to the medical assistant in the doctor's office. In a short decade and a half the association has:

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- Cooperated with AMA in public relations efforts beneficial to the medical profession as a whole.

But our work cannot stop here. As the only national association for medical assistants, AAMA is eager to contribute to advancement of this allied health field. We would like to share our educational programs with all of the medical assistants across the nation. But to do this we need the co-operation of many more physicians.

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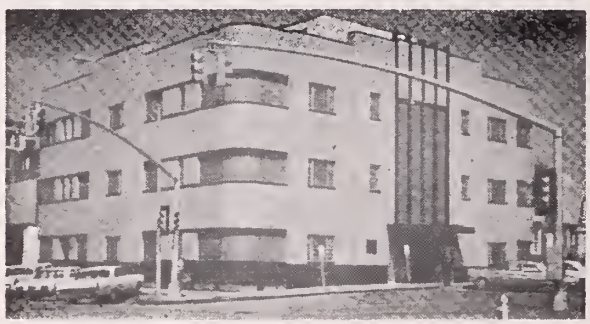
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The JOURNAL
of the Oklahoma State Medical Association

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August Issue

Editorial, Scientific, Book Reviews ... June 15, 1972
Advertising Copy ... July 15, 1972
News Copy, Miscellaneous Ads ... August 1, 1972

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Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reve ble in most instances by proper dosage adjustment, but are also occasionally o served at the lower dosage ranges. In a few instances syncope has been report Also encountered are isolated instance skin eruptions, edema, minor menstru irregularities, nausea and constipation, extrapyramidal symptoms, increased ar decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-volta fast activity) may appear during and aft treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasio ally, making periodic blood counts and liver function tests advisable during protracted therapy.
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JOURNAL

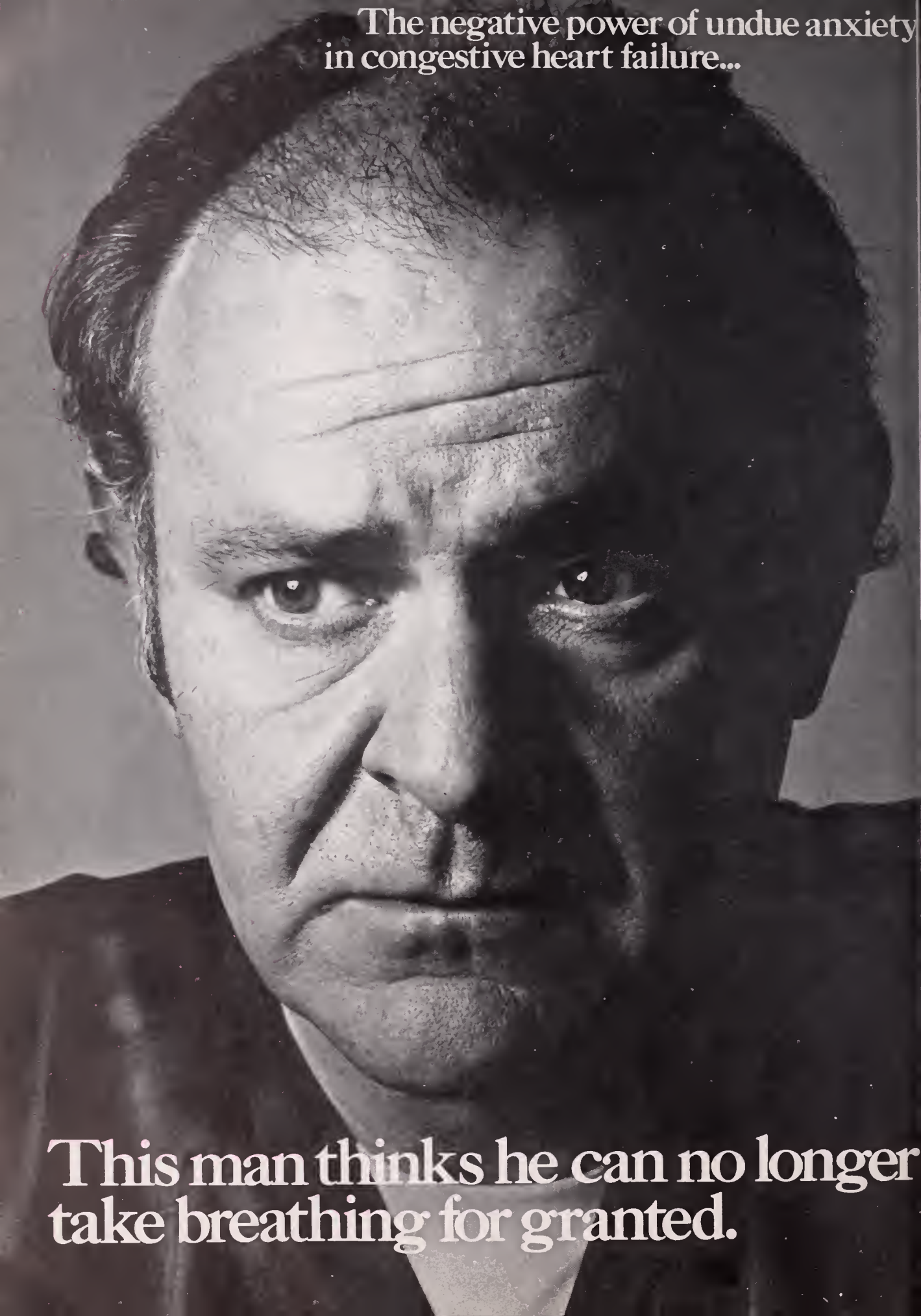
BALCONY

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STANLEY R. McCAMPBELL, MD


The negative power of undue anxiety
in congestive heart failure...
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take breathing for granted.

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Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

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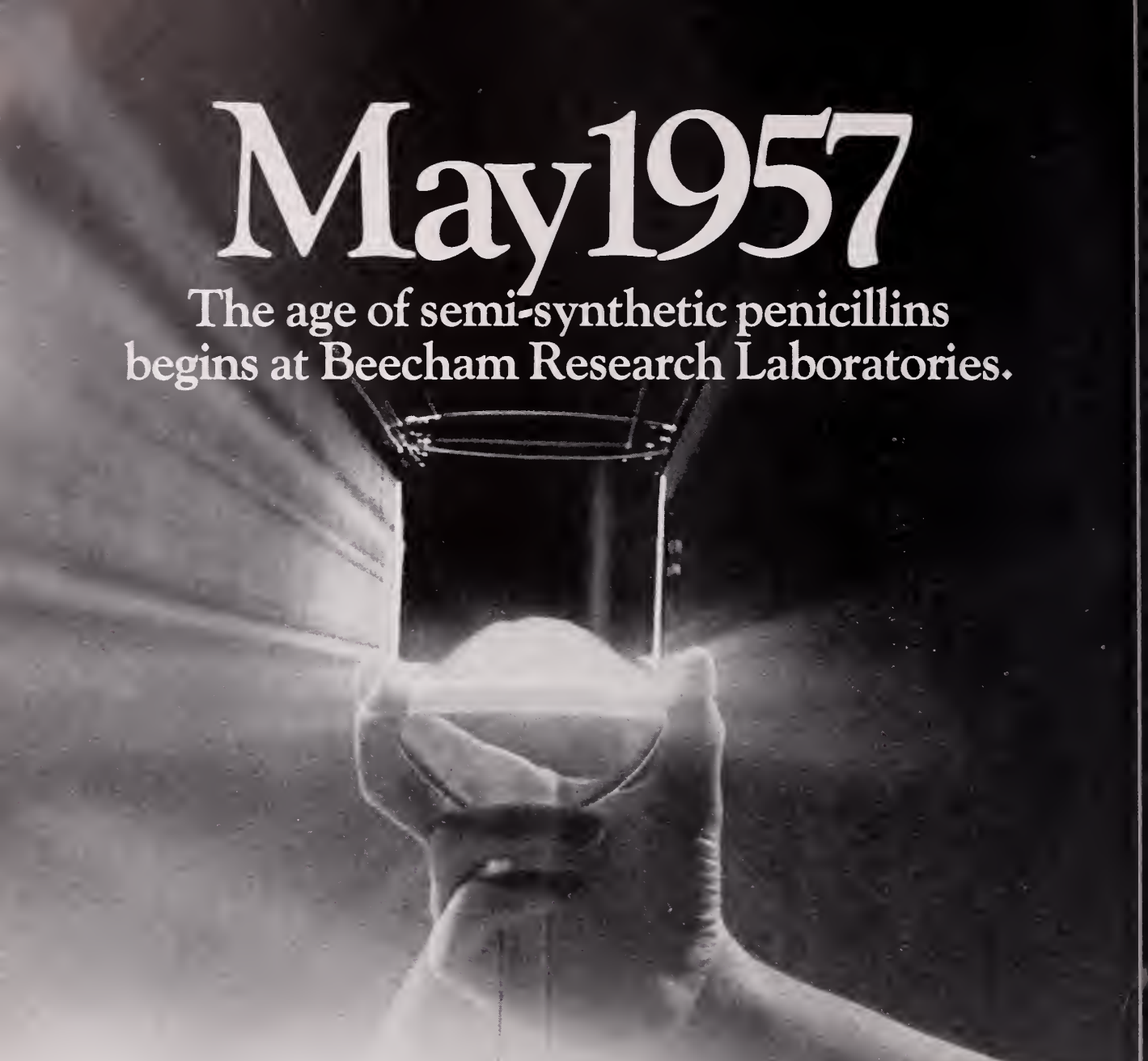
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MAY
1972
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"The history of science, and in particular the history of medicine... is... the history of man's reactions to the truth, the history of the gradual revelation of truth, the history of the gradual liberation of our minds from darkness and prejudice."

– George Sarton, from "The History of Medicine Versus the History of Art"

Should nongovernment scientists and physicians play a role in drug regulation?

Opinion

Results of a questionnaire to 7000 physicians:

82.8%
Physicians should play a role

78.3%
Independent scientists should play a role

69.8%
Medical academicians should play a role

Opinion & Dialogue

Dialog

Should nongovernment scientists and physicians play a role in drug regulation?

Doctor of Medicine

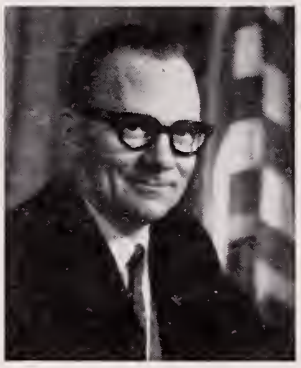
Herbert L. Ley, Jr., M.D., M.P.H., Formerly Commissioner, F.D.A. (1968-1969) Currently Medical Consultant

In order for drug regulation to be effective, participation in the regulatory process from nongovernment physicians and scientists must be encouraged. Without such involvement, there will continue to be a high degree of controversy surrounding any regulations promulgated by the Food and Drug Administration.

There are two areas in which participation and communication by nongovernment physicians and scientists could significantly improve the process of regulation. First, scientists and physicians throughout the country could become involved in consulting relationships with the Food and Drug Administration in important scientific areas while regulatory policies are being evolved. If nongovernment professionals could bring their expertise and experience to bear early in the decision-making process, they would have less reason to criticize the final outcome.

Secondly, practicing physicians, academic physicians, and academic-based scientists could make it their business to comment on proposed regulations appearing in the Federal Register. Ideally, a system could be instituted whereby medical, scientific and technical people could see the Federal Register regularly, and provide the Food and Drug Administration with a body of opinion that has so far gone unheard. The FDA is caught among pressures from industry, Congress, the Presidential Administration and consumers. It should also feel pressures from practicing physicians and scientists.

In order to become more involved in these stages of the drug regulatory process, nongovernment physicians and scientists should begin to exercise their influence through their respective professional organizations,



state and national medical societies, and specialty groups. Logically, a letter from these organizations representing a collective opinion has far greater weight in the regulatory process than individual letters. If the Food and Drug Administration receives opinions from these organizations early, before a regulation gets into the Federal Register, they are in a good position to respond with further study and review. Without such dissenting opinions, there is very little incentive to make changes in proposed regulations.

One instance in which practitioners did influence drug regulatory affairs in this way is the recent controversy that arose over the legitimacy of drug combinations. The strong opinion of practitioners on the value of such medication in clinical practice played a very prominent role in making the Food and Drug Administration modify its rather restrictive policy.

Another way in which practitioners can effectively influence drug regulations is by working with drug manufacturers conducting clinical trials of chemotherapeutic agents. When a drug is rated other than effective it may only mean that there is a lack of controlled clinical evidence as to efficacy. Thus, physicians might offer to conduct clinical studies that could help keep a truly effective drug in the marketplace. The treatment of diseases such as diabetes and angina are areas where the practitioner can aid in clinical studies because patients suffering from these diseases are rarely found in the conventional hospital setting.

By working with ethically and scientifically sound study designs in his everyday practice, the practitioner could begin to play an important part in determining official ratings on drug efficacy.

Nongovernment physicians and scientists and the FDA should also improve their lines of communication to the public. The medical community must develop a voice every bit as loud as that of the consumerists, the press, and others who sometimes criticize without complete information. If not, much of what the medical community *and* federal regulators do will often be represented in simplistic and somewhat misleading terms.

One illustration of the misuse of the media in this regard is the recall of anticoagulant drugs several years ago. This FDA action was given publicity by the press and television that went far beyond its probable importance. The result was a very uncomfortable situation for the practitioner who had patients taking these medications. Since the practitioner and pharmacist had not been informed of the action by the time it was publicized, in most states they were deluged with calls from worried patients.

The practitioner can attempt to solve these problems of inadequate communication in several ways. One would be the creation of a communications line in state pharmacy societies. When drug regulation news is to be announced, the society could immediately distribute a message to every pharmacist in the state. The pharmacist, in turn, could notify the physicians in his local community so that he and the physician could be prepared to answer inquiries from patients. Another approach would be to use professional publications the practitioner receives.

All of this leads back to my opening contention: if drug regulation is to be effective, timely, and related to the realities of clinical practice, a better method of communication and feedback must be developed between the nongovernmental medical and scientific communities and the regulatory agency.

ue

Maker of Medicine



Henry W. Gadsden, Chairman & Chief Executive Officer, Merck & Co., Inc.

In my opinion, it is the responsibility of all physicians and medical scientists to take whatever steps they think are desirable in a law- and regulation-making process that can have far-reaching impact on the practice of medicine. Yet many events in the recent past indicate that this is not happening. For example, it is apparent from drug efficacy studies that the NAS/NRC panels gave little consideration to the evidence that could have been provided by practicing physicians.

There are several current developments that should increase the concern of practicing physicians about drug regulatory affairs. One is the proliferation of malpractice claims and litigation. Another is the effort by government to establish the relative efficacy of drugs. This implies that if a physician prescribes a drug other than the "established" drug of choice, he may be accused of practicing something less than first-class medicine. It would come perilously close to federal direction of how medicine should be practiced.

In order to minimize this kind of arbitrary federal action, a way must be found to give practitioners both voice and representation in government affairs. Government must be caused to recognize the essentiality of seeking their views. One of the difficulties today, however, is that there is no way for concerned practitioners to participate in the early stages of decision-making processes. They usually don't hear about regulations until a proposal appears in the Federal Register, if then. By that time a lot of concrete has been poured, and a lot of boots are in the concrete.

Physicians in private practice, and particularly clinicians, should press for representation on the advisory committees of the Food and Drug Administration, joining with academic and teaching hospital physicians and scientists who are already serving. Though practitioners may not have access to all available information, the value of their clinical experience should be recognized. Clinicians, for example, rightly remind us that difficulty in *proving* precise effects does not necessarily mean a drug is ineffective.

Unless practitioners are more involved in drug regulations, it will be increasingly difficult for the pharmaceutical industry and scientists elsewhere to make optimal progress in drug development. The benefit/risk ratio must be re-emphasized, and as part of this it must be acknowledged that benefit can come from the judgments of medical science as a whole. Even this concept, unfortunately, is not always accepted in drug regulatory processes. For example, if current medical opinion holds that an excess of total lipids and cholesterol in the blood is probably predisposing to atherosclerosis, and if a drug is discovered which reduces total lipids and cholesterol, the drug ought to be accepted *prima facie* as a contribution to medical science . . . until someone disproves the theory. The sponsor should not have to prove the theory as well as to develop and test the drug.

I feel a major new effort must also be made to erase the feeling of mistrust of medicine and of medicines that seems to be growing in the public consciousness. Triggered primarily by strident announcements in Washington, people are reading and hearing confidence-shaking things almost continuously. Although challenge and awareness are essential to medical advancement, our long-term goal is constructively to build, not destroy. This means strengthening patient-physician relationships based on mutual confidence and trust. And in matters of health policy, it means working toward participatory rather than adversary proceedings—where everyone with an interest and a capacity to contribute has an opportunity to be heard . . . and, if that opportunity is not spontaneously afforded him, he may seek it.

Opinion & Dialogue

What is your opinion, doctor?
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Warnings: When weight loss is unsatisfactory the recommended dosage should not be increased in an attempt to obtain increased anorexigenic effect; discontinue the drug. Tolerance to the anorectic effect may develop. Drowsiness or stimulation may occur and may impair ability to engage in potentially hazardous activities such as operating machinery, driving a motor vehicle, or performing tasks requiring precision work or critical judgment. Therefore, such patients should be cautioned accordingly. Caution must be exercised if Pre-Sate (chlorphentermine hydrochloride) is used concomitantly with other central nervous system stimulants. There have been reports of pulmonary hypertension in patients who received related drugs.

Drug Dependence: Drugs of this type have a potential for abuse. Patients have been known to increase the intake of drugs of this type to many times the dosages recommended. In long-term controlled studies with high dosages of Pre-Sate, abrupt cessation did not result in symptoms of withdrawal.

Usage In Pregnancy: The safety of Pre-Sate (chlorphentermine hydrochloride) in human pregnancy has not yet been clearly established. The use of anorectic agents by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and child. Use of the drug during lactation is not recommended. Mammalian reproductive and teratogenic studies with high multiples of the human dose have been negative.

Usage In Children: Not recommended for use in children under 12 years of age.

Precautions: In patients with diabetes mellitus there may be alteration of insulin requirements due to dietary restrictions and weight loss. Pre-Sate (chlorphentermine hydrochloride) should be used with caution when obesity complicates the management of patients with mild to moderate cardiovascular disease or diabetes mellitus, and only when dietary restriction alone has been unsuccessful in achieving desired weight reduction. In prescribing this drug for obese patients in whom it is undesirable to introduce CNS stimulation or pressor effect, the physician should be alert to the individual who may be overly sensitive to this drug. Psychologic disturbances have been reported in patients who concomitantly receive an anorexic agent and a restrictive dietary regimen.

Adverse Reactions: Central Nervous System: When CNS side effects occur, they are most often manifested as drowsiness or sedation or overstimulation and restlessness. Insomnia, dizziness, headache, euphoria, dysphoria, and tremor may also occur. Psychotic episodes, although rare, have been noted even at recommended doses. **Cardiovascular:** tachycardia, palpitation, elevation of blood pressure. **Gastrointestinal:** nausea and vomiting, diarrhea, unpleasant taste, constipation. **Endocrine:** changes in libido, impotence. **Autonomic:** dryness of mouth, sweating, mydriasis. **Allergic:** urticaria. **Genitourinary:** diuresis and, rarely, difficulty in initiating micturition. **Others:** Paresthesias, sural spasms.

Dosage and Administration: The recommended adult daily dose of Pre-Sate (chlorphentermine hydrochloride) is one tablet (equivalent to 65 mg chlorphentermine base) taken after the first meal of the day. Use in children under 12 not recommended.

Overdosage: Manifestations: Restlessness, confusion, assaultiveness, hallucinations, panic states, and hyperpyrexia may be manifestations of acute intoxication with anorectic agents. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension, or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.

Management: Management of acute intoxication with sympathomimetic amines is largely symptomatic and supportive and often includes sedation with a barbiturate. If hypertension is marked, the use of a nitrate or rapidly acting alpha-receptor blocking agent should be considered. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard.

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(chlorphentermine HCl)

the trend is toward our kind of anorectic



Not a controlled drug under the Comprehensive Drug Abuse Prevention and Control Act

- low potential for abuse
- less CNS stimulation than with d-amphetamine or phenmetrazine

Effective anorectic adjunct to your program of caloric restriction and diet re-education

- weight loss comparable to d-amphetamine and phenmetrazine, superior to placebo
- convenient one-a-day dosage

PR-GP-21-B/W

Pre-Sate® (chlorphentermine HCl)...the increasingly practical appetite suppressant







T_4 IS THE PREDICTABLE HORMONE BECAUSE IT LOVES PROTEIN.

SYNTHROID® (sodium levothyroxine) is pure synthetic T_4, the major circulating thyroid hormone. It is reliable to use because of its affinity for protein-binding sites in the blood. T_3 is more fickle. Sometimes it binds. Sometimes it doesn't. T_4 more *predictably* binds to protein.

ALL THYROID-FUNCTION TESTS ARE USEFUL IN MONITORING SYNTHROID THERAPY

No calculations are needed, test interpretation is simple.

Any of the commonly used T_4 thyroid function tests (P.B.I., T_4 By Column, Murphy-Pattee, Free Thyroxine) are useful in monitoring patients on T_4 because they *all* measure T_4. Patients on SYNTHROID are thereby easy to monitor because their results will fall within predictable, elevated test ranges. Of course, clinical assessment is the best criterion of the thyroid status of the drug-treated patient.

TEST	HYPOTHYROID	SYNTHROID THERAPEUTIC NORMAL
P.B.I.	Less than 4 mcg %	6-10 mcg %
T_4 By Column	Less than 3 mcg %	7-9 mcg %
T_3 (Resin)	Less than 25%	27-35%
T_3 (Red Cell)	Less than 11%	11.5-18%
Free Thyroxine	Less than 0.7 nanograms %	0.7-2.5 nanograms %
Murphy-Pattee	Less than 2.9 mcg %	4-11 mcg %

TWO GOOD REASONS WHY THE ROAD TO NORMALIZED THYROID STATUS IS SO SMOOTH FOR THE SYNTHROID PATIENT.

(1) The onset of action of T_4 is gradual. It has a long in vivo "half-life" of over six days. (Occasional missed doses or accidental double-doses are of less concern because of this factor)[1]; (2) since SYNTHROID contains only T_4, the potential for metabolic surges traceable to more potent iodides (T_3) is eliminated.



AS WITH ANY THYROID PREPARATION, CAUTIOUS OBSERVATION OF THE PATIENT DURING THE BEGINNING OF THERAPY WILL ALERT THE PHYSICIAN TO ANY UNTOWARD EFFECTS.

Side effects, when they do occur, are related to excessive dosage. Caution should be exercised in administering the drug to patients with cardiovascular disease. Read the accompanying prescribing information for additional data or write Flint Laboratories.

Choose the Smooth Road ...to thyroid replacement therapy





PATIENTS CAN BE SUCCESSFULLY MAINTAINED ON A DRUG CONTAINING THYROXINE ALONE.

Thyroxine (T_4) is, as you know, the major circulating hormone produced by the thyroid gland. T_3 is also produced, in smaller amounts, and is active at the cellular level. For years it has been a working hypothesis among endocrinologists that T_4 is converted by the body to T_3. In 1970 this process, called "deiodination," was demonstrated by Braverman, Ingbar, and Sterling[2]. T_4 does convert to T_3, though the precise quantities are still being studied.

The conversion has been clinically demonstrated during the administration of T_4 to athyrotic patients. Their thyroid status is normalized on SYNTHROID alone, yet the presence of T_3 in these patients has been clearly shown.

WHY DOES SYNTHROID COST LESS THAN SYNTHETIC DRUGS CONTAINING T_3?

Very simple. T_3 costs more to make synthetically than does T_4. So it is economically necessary for a synthetic thyroid medication containing T_3 to cost more than one containing T_4 alone. Synthetic combinations cost patients nearly 50% more than SYNTHROID[3] because the T_3 costs more to start with; also there is the additional expense of formulating a tablet containing two active ingredients.

1. Latiolais, C. J., and Berry, C. C.: Misuse of Prescription Medications by Outpatients, *Drug Intelligence & Clin. Pharm.* 3:270-7, 1969.
2. Braverman, L. E., Ingbar, S. H., and Sterling, K.: Conversion of Thyroxine (T4) to Triiodothyronine (T3) in Athyreotic Human Subjects, *J. Clin. Invest.* 49:855-64, 1970.
3. American Druggist BLUEBOOK, March, 1971.

Synthroid®
(sodium levothyroxine)

THE FACTS ARE CLEAR AND HERE IS OUR OFFER.

FACTS:
Synthetic thyroid drugs are an improvement over animal gland products. Patients, even athyrotic ones, can be completely maintained on SYNTHROID (T_4) alone. Thyroid function tests are easy to interpret since they are *predictably* elevated when the patient adheres to SYNTHROID. Of all synthetic thyroid drugs, SYNTHROID is the most economical to the patient.

A

OFFER:
Free TAB-MINDER medication dispensers to start or convert all your hypothyroid patients to SYNTHROID. Free information to physicians on role of thyroid function tests in a new booklet titled: "Guideposts to Thyroid Therapy." Ask us.

Name _____

Address _____

City _____ State _____ Zip _____

Indications: SYNTHROID (sodium levothyroxine) is specific replacement therapy for diminished or absent thyroid function resulting from primary or secondary atrophy of the gland, congenital defect, surgery, excessive radiation, or antithyroid drugs. Indications for SYNTHROID (sodium levothyroxine) **Tablets** include myxedema, hypothyroidism without myxedema, hypothyroidism in pregnancy, pediatric and geriatric hypothyroidism, hypopituitary hypothyroidism, simple (nontoxic) goiter, and reproductive disorders associated with hypothyroidism. SYNTHROID (sodium levothyroxine) **for Injection** is indicated for intravenous use in myxedematous coma and other thyroid dysfunctions where rapid replacement of the hormone is required. The injection is also indicated for intramuscular use in cases where the oral route is suspect or contraindicated due to existing conditions or to absorption defects, and when a rapid onset of effect is not desired.

Precautions: As with other thyroid preparations, overdosage may cause diarrhea or cramps, nervousness, tremors, tachycardia, vomiting and continued weight loss. These effects may begin after four or five days or may not become apparent for one to three weeks. Patients receiving the drug should be observed closely for signs of thyrotoxicosis. If indications of overdosage appear, discontinue medication for 2-3 days, then resume at a lower dosage level. In patients with diabetes mellitus, careful observations should be made for changes in insulin or other antidiabetic drug dosage requirements. If hypothyroidism is accompanied by adrenal insufficiency, as Addison's Disease (chronic subcortical insufficiency), Simmonds's Disease (panhypopituitarism) or Cushing's syndrome (hyperadrenalism), these dysfunctions must be corrected prior to and during SYNTHROID (sodium levothyroxine) administration. The drug should be administered with caution to patients with cardiovascular disease; development of chest pains or other aggravations of cardiovascular disease requires a reduction in dosage.

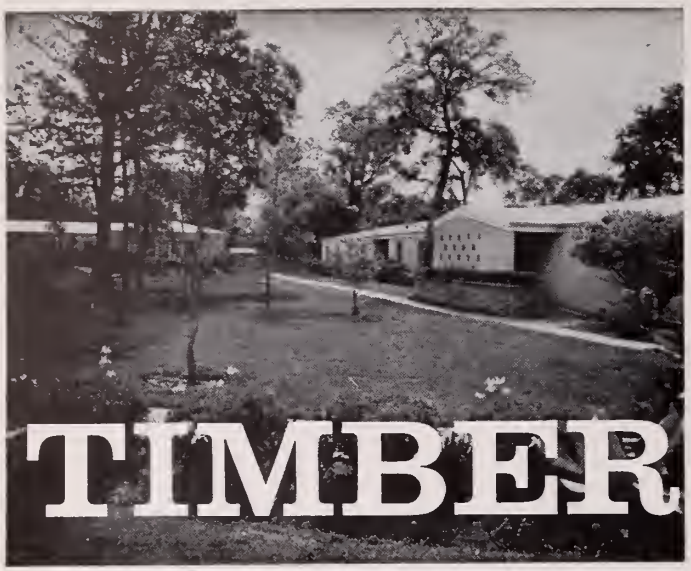
Contraindications: Thyrotoxicosis, acute myocardial infarction. **Side effects:** The effects of SYNTHROID (sodium levothyroxine) therapy are slow in being manifested. Side effects, when they do occur, are secondary to increased rates of body metabolism; sweating, heat palpitations with or without pain, leg cramps, and weight loss. Diarrhea, vomiting, and nervousness have also been observed. Myxedematous patients with heart disease have died from abrupt increases in dosage of thyroid drugs. Careful observation of the patient during the beginning of any thyroid therapy will alert the physician to any untoward effects.

In most cases with side effects, a reduction of dosage followed by a more gradual adjustment upward will result in a more accurate indication of the patient's dosage requirements without the appearance of side effects.

Dosage and Administration: The activity of a 0.1 mg SYNTHROID (sodium levothyroxine) TABLET is equivalent to approximately one grain thyroid, U.S.P. Administer SYNTHROID tablets as a single daily dose preferably after breakfast. In hypothyroidism without myxedema, the usual initial adult dose is 0.1 mg. daily and may be increased by 0.1 mg. every 30 days until proper metabolic balance is attained. Clinical evaluation should be made monthly and PBI measurement about every 90 days. Final maintenance dosage will usually range from 0.2-0.4 mg. daily. In adult myxedema, starting dose should be 0.025 mg. daily. The dose may be increased to 0.05 mg. after two weeks and to 0.1 mg. at the end of a second two weeks. The daily dose may be further increased at two-month intervals by 0.1 mg. until the optimum maintenance dose is reached (0.1-1.0 mg. daily).

Supplied: Tablets: 0.025 mg., 0.05 mg., 0.1 mg., 0.15 mg., 0.2 mg., 0.3 mg., 0.5 mg., scored and color-coded in bottles of 100, 500, and 1000. Injection: 500 mcg lyophilized active ingredient and 10 mg. of Mannitol N.F., in 10 ml. single-dose vial, with 5 ml. vial of Sodium Chloride Injection, U.S.P., as a diluent. SYNTHROID (sodium levothyroxine) **for Injection** may be administered intravenously utilizing 200-400 mcg of a solution containing 100 mcg. per ml. If significant improvement is not shown the following day, a repeat injection of 100-200 mcg. may be given.

FLINT LABORATORIES
DIVISION OF TRAVENOL LABORATORIES, INC
Morton Grove, Illinois 60053



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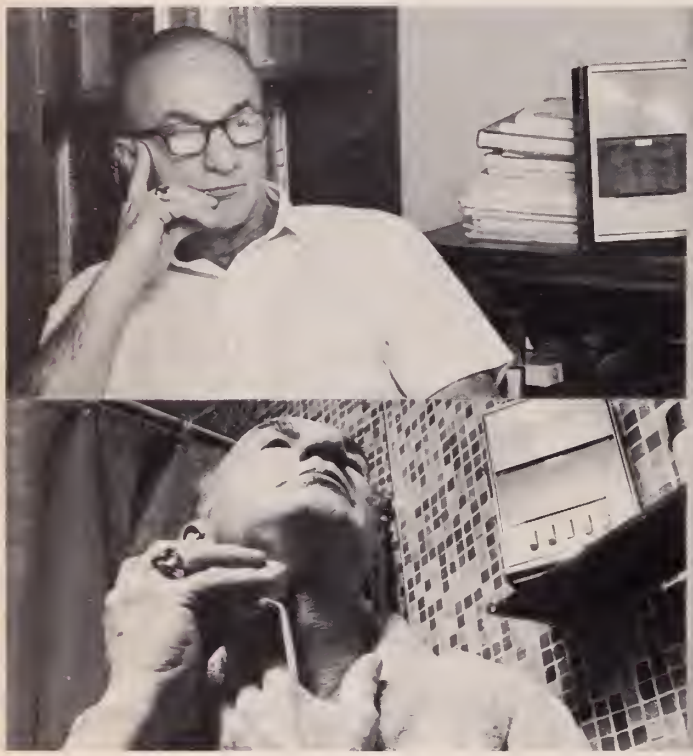
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Research Triangle Park
North Carolina 27709

A gratifying announcement about Empirin® Compound with Codeine



You may now specify up to five refills within six months when you prescribe Empirin Compound with Codeine (unless restricted by state law).

It is significant in this era of increased regulation, that Empirin Compound with Codeine has been placed in a less restrictive category. You may now wish to consider Empirin with Codeine even more frequently for its predictable analgesia in acute or protracted pain of moderate to severe intensity.

Empirin Compound with Codeine No. 3 contains codeine phosphate* (32.4 mg.) gr. ½. No. 4 contains codeine phosphate* (64.8 mg.) gr. 1. *(Warning—may be habit-forming.) Each tablet also contains: aspirin gr. 3½, phenacetin gr. 2½, caffeine gr. ½.



When you select this familiar antibiotic for IV infusion you have available a broad dosage range that hospitalized patients may need.

Intravenous Lincocin (lincomycin hydrochloride, Upjohn), with its 1.2 to 8 grams/day dosage range, covers many serious and even life-threatening infections. Lincocin is effective in infections due to susceptible strains of streptococci, pneumococci, and staphylococci. Lincocin IV therefore can be as useful in your hospitalized patients as its IM use has proved to be in your office patients. As with all antibiotics, *in vitro* susceptibility studies should be performed.

1.2 to 8 grams/day IV dosage range: Most hospitalized patients with uncomplicated pneumonias respond satisfactorily to 1.2 to 1.8 grams/day of Lincocin IV. These doses may have to be increased for more serious infections. In life-threatening situations as much as 8 grams/day has been administered intravenously to adults.

In usual IV doses, Lincocin (lincomycin hydrochloride, Upjohn) should be diluted in 250 ml or more of normal saline solution or 5% glucose in water. But when 4 grams or more per day is given, Lincocin should be diluted in not less than 500 ml of either solution, and the rate of administration should not exceed 100 ml/hour. Too rapid intravenous administration of doses exceeding 4 grams may result in hypotension or, in rare instances, cardiopulmonary arrest.

Effective gram-positive antibiotic: Lincocin IV is effective in respiratory tract, skin and soft-tissue, and bone

infections caused by susceptible strains of pneumococci, streptococci, and staphylococci, including penicillin-resistant strains. Staphylococcal strains resistant to Lincocin (lincomycin hydrochloride, Upjohn) have been recovered. Before initiating therapy, culture and susceptibility studies should be performed. Lincocin has proved valuable in treating patients hypersensitive to penicillin or cephalosporins, since Lincocin does not share antigenicity with these compounds. However, hypersensitivity reactions have been reported, some of these in patients known to be sensitive to penicillin.

Well tolerated at infusion site: Lincocin intravenous infusions have not produced local irritation or phlebitis, when given as recommended. Lincocin is usually well tolerated in patients who are hypersensitive to other drugs. Nevertheless, Lincocin should be used cautiously in patients with asthma or significant allergies.

In patients with impaired renal function, the recommended dose of Lincocin should be reduced to 25—30% of the dose for patients with normal kidney function. Its safety in pregnant patients and in infants less than one month of age has not been established.

Lincocin may be used with other antimicrobial agents: Since Lincocin is stable over a wide pH range, it is suitable for incorporation in intravenous infusions; it also may be administered concomitantly with other antimicrobial agents when indicated. However, Lincocin should not be used with erythromycin, as *in vitro* antagonism has been reported.

Lincocin®

Sterile Solution (300 mg per ml)

(lincomycin hydrochloride, Upjohn)

For further prescribing information, please see following page.



© 1972 The Upjohn Company



Sterile Solution (300 mg. per ml.)

Lincocin®

(lincomycin hydrochloride, Upjohn)

Up to 8 grams per day by IV infusion for hospitalized patients with life-threatening infections. Lincocin is effective in infections due to susceptible strains of streptococci, pneumococci, and staphylococci. As with all antibiotics, *in vitro* susceptibility studies should be performed.

Each preparation contains:	Lincomycin hydrochloride monohydrate equivalent to lincomycin base
250 mg Pediatric Capsule	250 mg
500 mg Capsule	500 mg
*Sterile Solution per 1 ml	300 mg
Syrup per 5 ml	250 mg

*Contains also: Benzyl Alcohol 9 mg; and, Water for Injection—q.s.

Lincocin (lincomycin hydrochloride) is indicated in infections due to susceptible strains of staphylococci, pneumococci, and streptococci. *In vitro* susceptibility studies should be performed. Cross resistance has not been demonstrated with penicillin, ampicillin, cephalosporins, chloramphenicol or the tetracyclines. Some cross resistance with erythromycin has been reported. Studies indicate that Lincocin does not share antigenicity with penicillin compounds.

CONTRAINDICATIONS: History of prior hypersensitivity to lincomycin or clindamycin. Not indicated in the treatment of viral or minor bacterial infections.

WARNINGS: *CASES OF SEVERE AND PERSISTENT DIARRHEA HAVE BEEN REPORTED AND HAVE AT TIMES NECESSITATED DISCONTINUANCE OF THE DRUG. THIS DIARRHEA HAS BEEN OCCASIONALLY ASSOCIATED WITH BLOOD AND MUCUS IN THE STOOLS AND HAS AT TIMES RESULTED IN AN ACUTE COLITIS. THIS SIDE EFFECT USUALLY HAS BEEN ASSOCIATED WITH THE ORAL DOSAGE FORM BUT OCCASIONALLY HAS BEEN REPORTED FOLLOWING PARENTERAL THERAPY.* A careful inquiry should be made concerning previous sensitivities to drugs or other allergens. Safety for use in pregnancy has not been established and Lincocin (lincomycin hydrochloride) is not indicated in the newborn. Reduce dose 25 to 30% in patients with severe impairment of renal function.

PRECAUTIONS: Like any drug, Lincocin should be used with caution in patients having a history of asthma or significant allergies. Overgrowth of nonsusceptible organisms, particularly yeasts, may occur and require appropriate measures. Patients with pre-existing monilial infections requiring Lincocin therapy should be given concomitant antimonilial treatment. During prolonged Lincocin therapy, periodic liver function studies and blood counts should be performed. Not recommended (inadequate data) in patients with pre-existing liver disease unless special clinical circumstances indicate. Continue treatment of β-hemolytic streptococci infections for 10 days to diminish likelihood of rheumatic fever or glomerulonephritis.

ADVERSE REACTIONS: *Gastrointestinal*—Glossitis, stomatitis, nausea, vomiting. Persistent diarrhea, enterocolitis, and pruritus ani. *Hemopoietic*—Neutropenia, leukopenia, agranulocytosis, and thrombocytopenic purpura have been reported. *Hypersensitivity reactions*—Hypersensitivity reactions such as angioneurotic edema, serum sickness, and anaphylaxis have been reported, sometimes in patients sensitive to penicillin. If allergic reaction occurs, discontinue drug. Have epinephrine, corticosteroids, and antihistamines available for emergency treatment. *Skin and mucous membranes*—Skin rashes, urticaria, vaginitis, and rare instances of exfoliative and vesiculobullous dermatitis have been reported. *Liver*—Although no direct relationship to liver dysfunction is established, jaundice and abnormal liver function tests (particularly serum transaminase) have been observed in a few instances. *Cardiovascular*—Instances of hypotension following parenteral administration have been reported, particularly after too rapid IV administration. Rare instances of cardiopulmonary arrest have been reported after too rapid IV administration. If 4.0 grams or more administered IV, dilute in 500 ml of fluid and administer no faster than 100 ml per hour. *Special senses*—Tinnitus and vertigo have been reported occasionally. *Local reactions*—Excellent local tolerance demonstrated to intramuscularly administered Lincocin (lincomycin hydrochloride). Reports of pain following injection have been infrequent. Intravenous administration of Lincocin in 250 to 500 ml of 5% glucose in distilled water or normal saline has produced no local irritation or phlebitis.

HOW SUPPLIED: *250 mg* and *500 mg* Capsules—bottles of 24 and 100. *Sterile Solution, 300 mg per ml*—2 and 10 ml vials and 2 ml syringe. *Syrup, 250 mg per 5 ml*—60 ml and pint bottles.

For additional product information, consult the package insert or see your Upjohn representative.

MED B-6-S (KZL-7) JA71-1631

The Upjohn Company
Kalamazoo, Michigan 49001

Upjohn



rheumatoid arthritic blowup...

Tandearil® Geigy

oxyphenbutazone NF

tablets of 100 mg.

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral lesions (symptoms of blood dyscrasia); dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.
Indications: Acute gouty arthritis, rheumatoid arthritis, rheumatoid spondylitis.
Contraindications: Children 14 years or less; senile patients; history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypertension; thyroid disease; systemic edema; stomatitis and salivary gland enlargement due to the drug; polymyalgia rheumatica and temporal arteritis; patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.
Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpredictable benefits against potential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.
Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.
Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angiitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement.
(B)98-146-800-E

For complete details, including dosage, please see full prescribing information.

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardsley, New York 10502

TA-8356-9



a new outlook in chronic pain

of moderate to severe intensity

Though Talwin® can be compared to codeine in analgesic efficacy, it is not a narcotic. So patients receiving Talwin for prolonged periods face fewer of the consequences you've come to expect with narcotic analgesics. And that, in the long run, can mean a better outlook for your chronic-pain patient.

Talwin Tablets are:

- **Comparable to codeine in analgesic efficacy:** one 50 mg. Talwin Tablet appears equivalent in analgesic effect to 60 mg. (1 gr.) of codeine. Onset of significant analgesia usually occurs within 15 to 30 minutes. Analgesia is usually maintained for 3 hours or longer.
- **Tolerance not a problem:** tolerance to the analgesic effect of Talwin Tablets has not been reported, and no significant changes in clinical laboratory parameters attributable to the drug have been reported.
- **Dependence rarely a problem:** during three years of wide clinical use, only a few cases of dependence have been reported. In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in dose by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain.
- **Not subject to narcotic controls:** convenient to prescribe – day or night – even by phone.
- **Generally well tolerated by most patients:** infrequently cause decrease in blood pressure or tachycardia; rarely cause respiratory depression or urinary retention; seldom cause diarrhea or constipation. If dizziness, lightheadedness, nausea or vomiting are encountered, these effects tend to be self-limiting and to decrease after the first few doses. (See last page of this advertisement for a complete discussion of adverse reactions and a brief discussion of other Prescribing Information.)

50 mg. Tablets

Talwin®

brand of

pentazocine (as hydrochloride)

the long-range analgesic

a new outlook in chronic pain

of moderate to severe intensity



Contraindications: Talwin, brand of pentazocine (as hydrochloride), should not be administered to patients who are hypersensitive to it.

Warnings: *Head Injury and Increased Intracranial Pressure.* The respiratory depressant effects of Talwin and its potential for elevating cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a preexisting increase in intracranial pressure. Furthermore, Talwin can produce effects which may obscure the clinical course of patients with head injuries. In such patients, Talwin must be used with extreme caution and only if its use is deemed essential.

Usage in Pregnancy. Safe use of Talwin during pregnancy (other than labor) has not been established. Animal reproduction studies have not demonstrated teratogenic or embryotoxic effects. However, Talwin should be administered to pregnant patients (other than labor) only when, in the judgment of the physician, the potential benefits outweigh the possible hazards. Patients receiving Talwin during labor have experienced no adverse effects other than those that occur with commonly used analgesics. Talwin should be used with caution in women delivering premature infants.

Drug Dependence. There have been instances of psychological and physical dependence on parenteral Talwin in patients with a history of drug abuse and, rarely, in patients without such a history. Abrupt discontinuance following the extended use of parenteral Talwin has resulted in withdrawal symptoms. There have been a few reports of dependence and of withdrawal symptoms with orally administered Talwin. Patients with a history of drug dependence should be under close supervision while receiving Talwin orally.

In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in dose by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain.

Acute CNS Manifestations. Patients receiving therapeutic doses of Talwin have experienced, in rare instances, hallucinations (usually visual), disorientation, and confusion which have cleared spontaneously within a period of hours. The mechanism of this reaction is not known. Such patients should be very closely observed and vital signs checked. If the drug is reinstituted it should be done with caution since the acute CNS manifestations may recur.

Usage in Children. Because clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Ambulatory Patients. Since sedation, dizziness, and occasional euphoria have been noted, ambulatory patients should be warned not to operate machinery, drive cars, or unnecessarily expose themselves to hazards.

Precautions: *Certain Respiratory Conditions.* Although respiratory depression has rarely been reported after oral administration of Talwin, the drug should be administered with caution to patients with respiratory depression from any cause, severe bronchial asthma and other obstructive respiratory conditions, or cyanosis.

Impaired Renal or Hepatic Function. Decreased metabolism of the drug by the liver in extensive liver disease may predispose to accentuation of side effects. Although laboratory tests have not indicated that Talwin causes or increases renal or hepatic impairment, the drug should be administered with caution to patients with such impairment.

Myocardial Infarction. As with all drugs, Talwin should be used with caution in patients with myocardial infarction who have nausea or vomiting.

Biliary Surgery. Until further experience is gained with the effects of Talwin on the sphincter of Oddi, the drug should be used with caution in patients about to undergo surgery of the biliary tract.

Patients Receiving Narcotics. Talwin is a mild narcotic antagonist. Some patients previously receiving narcotics have experienced mild withdrawal symptoms after receiving Talwin.

CNS Effect. Caution should be used when Talwin is administered to patients prone to seizures; seizures have occurred in a few such patients in association with the use of Talwin although no cause and effect relationship has been established.

Adverse Reactions: Reactions reported after oral administration of Talwin include *gastrointestinal:* nausea, vomiting; infrequently constipation; and rarely abdominal distress, anorexia, diarrhea. *CNS effects:* dizziness, lightheadedness, sedation, euphoria, headache; infrequently weakness, disturbed dreams, insomnia, syncope, visual blurring and focusing difficulty, hallucinations (see *Acute CNS Manifestations* under WARNINGS); and rarely tremor, irritability, excitement, tinnitus. *Autonomic:* sweating; infrequently flushing; and rarely chills. *Allergic:* infrequently rash; and rarely urticaria, edema of the face. *Cardiovascular:* infrequently decrease in blood pressure, tachycardia. *Other:* rarely respiratory depression, urinary retention.

Dosage and Administration: *Adults.* The usual initial adult dose is 1 tablet (50 mg.) every three or four hours. This may be increased to 2 tablets (100 mg.) when needed. Total daily dosage should not exceed 600 mg.

When antiinflammatory or antipyretic effects are desired in addition to analgesia, aspirin can be administered concomitantly with Talwin.

Children Under 12 Years of Age. Since clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Duration of Therapy. Patients with chronic pain who have received Talwin orally for prolonged periods have not experienced withdrawal symptoms even when administration was abruptly discontinued (see WARNINGS). No tolerance to the analgesic effect has been observed. Laboratory tests of blood and urine and of liver and kidney function have revealed no significant abnormalities after prolonged administration of Talwin.

Overdosage: *Manifestations.* Clinical experience with Talwin overdosage has been insufficient to define the signs of this condition.

Treatment. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated. Assisted or controlled ventilation should also be considered. Although nalorphine and levallorphan are *not* effective antidotes for respiratory depression due to overdosage or unusual sensitivity to Talwin, parenteral naloxone (Narcan®, available through Endo Laboratories) is a specific and effective antagonist. If naloxone is not available, parenteral administration of the analeptic, methylphenidate (Ritalin®), may be of value if respiratory depression occurs.

Talwin is not subject to narcotic controls.

How Supplied: Tablets, peach color, scored. Each tablet contains Talwin (brand of pentazocine) as hydrochloride equivalent to 50 mg. base. Bottles of 100.

Winthrop Winthrop Laboratories, New York, N. Y. 10016 (1583)

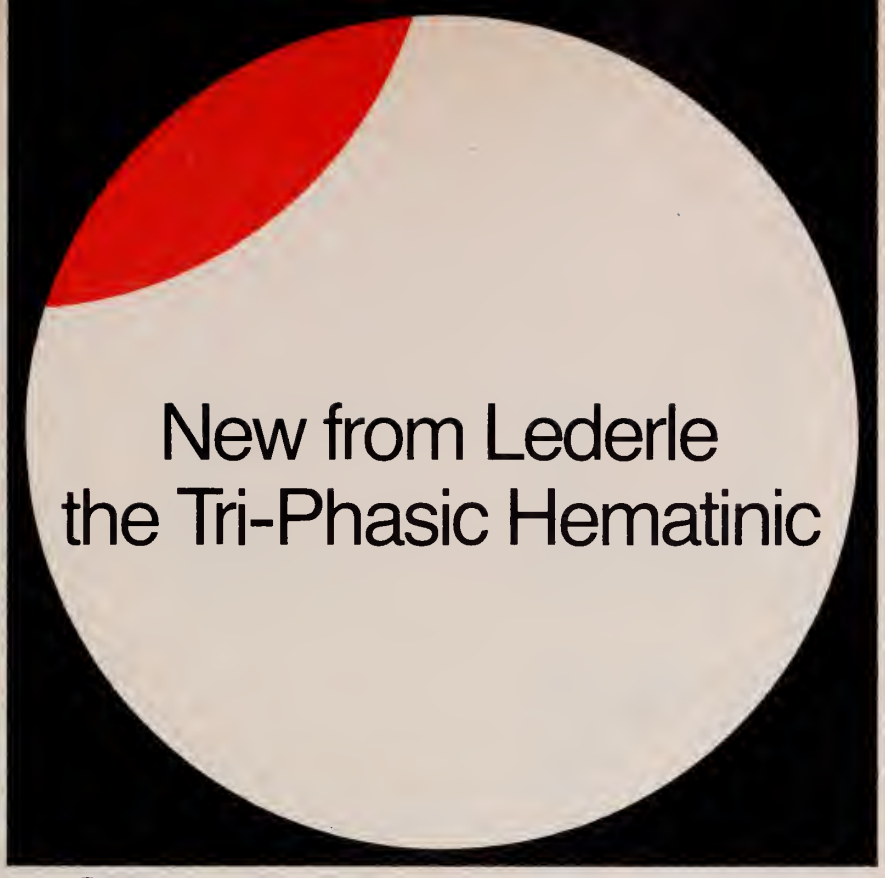
50 mg. Tablets

Talwin®

brand of

pentazocine (as hydrochloride)

the long-range analgesic



Specifically formulated with
vitamins and minerals important
in the treatment of anemia



PHASE 1
Enhanced Absorption

Each tablet provides 115 mg elemental iron as the highly absorbable ferrous fumarate *plus* 600 mg of Vitamin C.



PHASE 2
Erythrocyte Formation

Each tablet provides Vitamin B_{12} (25 mcg) and Folic Acid (1 mg) to replace deficiencies.



PHASE 3
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Each tablet provides Vitamin E, which may be involved in lessening red blood cell fragility.



For common anemias
as well as problem ones

TriHEMIC™ 600
HEMATINIC TABLETS

Tri-Phasic Hematinic with 600 mg Vitamin C PLUS Vitamin E

Each tablet contains:	
Vitamin C (Ascorbic Acid)	600 mg.
Vitamin B_{12} (Cobalamin Concentrate, N.F.)	25 mcg.
Intrinsic Factor Concentrate	75 mg.
Folic Acid	1 mg.
Vitamin E (*d*-Alpha Tocopheryl Acid Succinate)	30 Int. Units
Elemental Iron (as present in 350 mg. of Ferrous Fumarate)	115 mg.
Dioctyl Sodium Sulfosuccinate U.S.P.	50 mg.

Dosage: One Tablet Daily.
Available in Bottles of 30 Tablets.
On Your Prescription Only.



Precautions: Some patients affected with pernicious anemia may not respond to orally administered Vitamin B_{12} with intrinsic factor concentrate and there is no known way to predict which patients will respond or which patients may cease to respond. Periodic examinations and laboratory studies of pernicious anemia patients are essential and recommended. If any symptoms of intolerance occur, discontinue drug temporarily or permanently. Folic acid, especially in doses above 1 mg. daily, may obscure pernicious anemia, in that hematologic remission may occur while neurological manifestations remain progressive.

Adverse Reactions: G.I.: nausea, vomiting, diarrhea, abdominal pain. Skin rashes may occur. Such reactions may necessitate temporary or permanent changes in dosage or usage. Allergic sensitization has been reported following both oral and parenteral administration of folic acid.

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Tri-Phasic Hematinic with 600 mg Vitamin C PLUS Vitamin E

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421-1



if skin is infected, or open to infection...

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- low allergenic risk—prompt clinical response

Special Petrolatum Base
Neosporin® Ointment
(polymyxin B-bacitracin-neomycin)

Each gram contains: Aerosporin® brand polymyxin B sulfate, 5000 units; zinc bacitracin, 400 units; neomycin sulfate 5 mg. (equivalent to 3.5 mg. neomycin base); special white petrolatum q. s.
In tubes of 1 oz. and ½ oz. for topical use only.

Vanishing Cream Base
Neosporin®-G Cream
(polymyxin B-neomycin-gramicidin)

Each gram contains: Aerosporin® brand polymyxin B sulfate, 10,000 units; neomycin sulfate, 5 mg. (equivalent to 3.5 mg. neomycin base); gramicidin, 0.25 mg., in a smooth, white, water-washable vanishing cream base with a pH of approximately 5.0. Inactive ingredients: liquid petrolatum, white petrolatum, propylene glycol, polyoxyethyiene polyoxypropylene compound, emulsifying wax, purified water, and 0.25% methylparaben as preservative.
In tubes of 15 g.

NEOSPORIN for topical infections due to susceptible organisms, as in impetigo, surgical after-care, and pyogenic dermatoses.

Precaution: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Contraindications: Not for use in the external ear canal if the eardrum is perforated. These products are contraindicated in those individuals who have shown hypersensitivity to any of the components.

Complete literature available on request from Professional Services Dept. PML.

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- ☐ **belladonna alkaloids—for the hyperactive bowel**
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- ☐ **phenobarbital—for associated anxiety and tension**

Composition: Each chewable, fruit-flavored, scored tablet contains: 16 mg. phenobarbital (warning: may be habit-forming); 0.1 mg. hyoscyamine sulfate; 0.02 mg. atropine sulfate; 0.007 mg. scopolamine hydrobromide; 40 mg. simethicone.
Contraindications: Hypersensitivity to barbiturates or belladonna alkaloids, glaucoma, advanced renal or hepatic disease.
Precautions: Administer with caution to patients with incipient glaucoma, bladder neck obstruction or urinary bladder atony. Prolonged use of barbiturates may be habit-forming.
Side effects: Blurred vision, dry mouth, dysuria, and other atropine-like side effects may occur at high doses, but are only rarely noted at recommended dosages.
Dosage: Adults: One or two tablets three or four times daily. Dosage can be adjusted depending on diagnosis and severity of symptoms. Children 2 to 12 years: One half or one tablet three or four times daily. Tablets may be chewed or swallowed with liquids.

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(from the Greek **kinetikos,**
to move,
and the Latin **sedatus,**
to calm)

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antispasmodic/sedative/antiflatulent

Spring peeper (tree frog, *Hyla crucifer*): this small amphibian can expand its throat membrane with air until it is twice the size of its head.

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Grass Roots Cultivation

TAX SUPPORTED institutions which provide resources and programs for higher education are political entities. This is not to say that they belong to politicians; neither should they be directed, dominated nor unduly influenced by politicians or persons with political ambitions. But they are political in the sense that they are administered, albeit indirectly, by the body of people comprising the constituency of a state.

Political entities prosper in proportion to the support and commitment they secure from the body politic. Insofar as it represents the manifest will of a constituency, the support of politicians is also important to the prosperity of a political institution. The aggregate influence of those who elect and those elected constitutes "the grass roots," that botanical metaphor so frequently exercised in political campaigns.

Our Health Sciences Center is a tax supported institution . . . at least partially and, at best, inadequately, but nevertheless tax supported. It is therefore a political entity. And it is in deep trouble. Whether it is in trouble at the grass roots can only be assumed; that it is in trouble with our political leaders is a certainty. The basic cause of the trouble, today as in the past, is obscured by a publicized crisis complete with charges and counter-charges, misunderstanding and poor communication.

In analyzing the various causes of these chronic problems, it becomes quite apparent that our medical center simply has not established a significant rapport with the citizens and communities of our state. It has developed no basis of mutual respect and support with the practicing physicians in our cities and towns. It has virtually ignored the grass roots, through which it is nourished, and attempted instead to remain aloof or, under duress, deal directly with politicians at the State Capitol.

Obviously, such policies and attitudes have not succeeded. On the contrary, our medical center has survived in crisis since its earliest beginnings, suspended only by the raveling thread of political benevolence.

Such relationships must change . . . and change now. There are no options. The fiction of political independence and academic sovereignty must be eschewed. The practice of courting politicians must be supplemented if not supplanted by a dynamic, vigorous, unrelenting cultivation of the grass roots of our constituency. Our Health Sciences Center, its institutions, its programs and its people must become a real part of the lay and professional communities of our state. And concurrently, the needs and problems of these communities must become a principal, vital concern of the center.

These changes must and can be swiftly executed, but not without the active cooperation of each physician in the state. Your help is urgently needed by the staff and faculties of the center as they extend their efforts to cultivate the grass roots. Your wisdom is valuable and your guidance will be solicited. When it is, please give generously.—*MRJ* □

WHAT IS A DOCTOR?



He is a man who dedicates his life to helping people. No higher calling comes readily to mind.

He is a man with eight years of college education and most often five extra years of special training. While his contemporaries were doing the frivolous things of the young, he was preparing himself for his humanitarian purpose. This robbed him of his youth.

He is, literally, giving his life; for, he will die an average of eight years earlier than the general population. Add the thirteen years of education and the eight years of loss of longevity and this approximates the usual life time career of most Americans.

If you are his patient, he loves you like a brother. He would much rather cure you than to collect his fee for services he has provided. He would prefer that you were well and happy rather than complaining of problems. He represents the only profession that is trying to put itself out of business by preventive methods. He is expected to see through your false symptoms of pain and suffering and to know that your problems are really economic, disappointment in a loved one, or a lack of communication with your teenage child. Often, he sacrifices his personal relationships with his own family for others. This is the highest price you can ask of anyone.

He is working harder and harder, to give better and better service to the public. His product is unequalled anywhere in the world. Yet, he is often misunderstood, because the public tends to project their own motives onto him. He is on trial in the public eye every minute of every day and is expected to produce miracles routinely.

He is a human creature doing his very best day after day to do a difficult to impossible job so that others may benefit from his superb training. Above all he is human, with all the base traits that humans have. He is a man who is trusted more than is a governor, senator, judge, attorney, or businessman. Patients tell their doctor life secrets, which would not be divulged to others, knowing that they can depend on his monumental understanding and discretion. As Robert Louis Stevenson has said, the physician is the flower, such as it is, of our civilization, and he shares as little as any in the defects of the period.

WHY, THEN;

Are congressmen and senators elected who in turn criticize and destroy this man?

Are lesser human creatures, who do not measure up to the high standard that he has set for himself, allowed to tell him how he is to respond, to react, and how he is to be paid for his services?

After all, to whom is the doctor responsible other than himself, his patients, and his peers? □

Sincerely,

S. R. McCampbell, MD

OSMA JOURNAL/scientific

Nonanesthetic "After Loading" Techniques for Intracavitary Radiation Therapy of Carcinoma of the Cervix

T. J. BRICKNER, JR., MD
GEORGE H. KAMP, MD
DAVID S. GOODEN, PhD

Fully "after loaded" intracavitary radioactive material therapy for gynecological malignancies can be performed without anesthesia in nearly all cases.

THIS PAPER describes techniques and equipment for making highly individualized intracavitary applications of radioactive materials for the treatment of carcinoma of the cervix. The techniques described have the advantage of not requiring general anesthesia, reducing trauma to the tumor and reducing unnecessary radiation exposure to the physician and attending personnel.

The fundamental basis for intracavitary radiation therapy is the establishment of a high radiation dose in the tissue volume of the cervix, upper vaginal vault and the paracervical tissues. Due to the rapid fall off in radiation levels with increasing distance from the sources, normal tissues such as the bladder and rectum receive much less radiation. Cancer of the cervix was first treated with radium in 1908. Since that time intracavitary radiation therapy applications have become one of the basic modalities in treatment. Using this technique, radium or a similar isotope is placed in the endocervical canal, uterine cavity and vaginal vault. There are many different applicators and several different treatment techniques which are presently being used in this country. The Stockholm technique utilizes high intensity radiation fields to the tissues of interest. The Paris technique uses less intense radiation fields and longer applications, usually involving well over 100 hours. The Stockholm and Paris techniques were forerunners of present intracavitary techniques and they are still used in many areas for Stage I and Stage II carcinoma of the cervix. In the United States most intracavitary applicators and techniques are modifications of the Manchester System which was developed in the 1930's in England. This technique is somewhat intermediate between the above-mentioned systems.

The mechanics of the applications have led many therapists to design their own applicators. These have been designed to provide maximum flexibility and ease of mechanical insertion. Until recent years, radioactive sources were placed in the applicators prior to intracavitary insertion. This method has several disadvantages. There is a considerable radiation dose to the physician inserting the applicators and to attending personnel. Also due to the physician's knowledge of constant exposure there is psychological pressure to hurry during the

St. Francis Hospital, Tulsa, Oklahoma 74136.

course of the insertion. This does not allow the physician to take as much time as he might desire to obtain the best possible applicator placement. This also makes him less inclined to unpack and redo an application if radiographs reveal that less than optimum geometry was obtained during the first attempt.

These disadvantages have led to the development of "after loading" techniques. This allows applicators containing no radioactive material to be placed in the vaginal vault and intrauterine canal. The insertion is made and checked for proper positioning prior to the insertion of any radioactive materials. When the physician is fully satisfied with the placement of the applicators, the radioactive material can be loaded into place in the patient's room with very little exposure to the physician or attending staff.

Doctor Gilbert Fletcher of M. D. Anderson Hospital, Houston, Texas, has developed an excellent set of "after loading" applicators. With Doctor Fletcher's applicators, however, it is usually necessary to make the insertion in the operating room under general anesthesia. The necessity of general anesthesia is due to the passage of the uterine tandem which requires significant dilation of the cervical os. Also, the relaxation induced by anesthesia allows easy and full packing of the vaginal vault to force the bladder and rectum away from their natural proximity to the vaginal sources and to hold the applicators in place.

A significant contribution to "after loading" techniques has been made by Doctor G. Ray Ridings of St. Paul Hospital, Dallas, Texas. Doctor Ridings has developed a tandem for insertion through the cervical os which has an outside diameter of only four millimeters. This is the same diameter as the tip of the usual Sims sound. Thus, if the cervical os and uterine cavity can be sounded with usual techniques, the tandem can be applied without significant dilation. This can be done in nearly all cases with no anesthesia whatsoever and with only mild discomfort to the patient. There is an added advantage in that there is an absolute minimum of tumor manipulation.

For the past three years the nonanesthetic Ridings' techniques with some modifications have been used at St. Francis Hospital. Over 150 applications have been made using these techniques. We have been very pleased with the techniques and have found in most cases that with only mild sedation there is little discomfort to the patient. In approximately 5% to 10% of the patients who receive intracavitary applications it is necessary to use general anesthesia. This is usually for one of two reasons. First, in some cases the patients are extremely anxious and emotionally unstable to the point that they are unable to cooperate with the physician. This is quite unusual and has occurred only five times in the past three years. The second reason is that tumor growth has caused a marked derangement of anatomical structures within the vaginal vault. For these patients, anesthesia is required since the degree of manipulation required would prove quite painful.

Equipment used at St. Francis Hospital for intracavitary radiation therapy applications consists of several curvatures of Ridings' tandems and rectally shielded Fletcher "after loading" ovoids. Both of these items are commercially available.* In our institution, all intracavitary radiation therapy applications are made with radioactive cesium. Cesium is used because radiation safety is easier to accomplish with this material and rectal and bladder doses to the patient can be reduced. Several methods are used in providing dosimetry for intracavitary radiation therapy applications. These include monitoring rectal doses with thermoluminescence dositometers and performing complete computerized dosimetry. The specifics of a routine application which can be performed on a vast majority of patients are given in the following paragraphs.

The patient is seen as an outpatient and a history and physical are performed several days prior to admission. Any laboratory work required is ordered at this time and instructions are given regarding the patient's admission. Orders are written which include a liquid diet, bowel paralysis with "Lomotil" and paregoric, premedication with "Demerol" and a perineal wash and douche with "pHisoHex."

*Radium Chemical Company, Inc., 161 East 42nd Street, New York, New York 10017.

The patient reports to the hospital at about noon and is usually available for the Radiation Therapy Department between 1:00 and 1:30 p.m. the same day. The patient is given an injection of "Demerol" and "Phenergan" and brought to the department and placed on a GYN examining table or, in our case, a Model K-11 therapy couch by Koenigkramer. This therapy couch is used as an examining table and operating table. Since it is mounted on wheels, the patient can be taken to the X-ray Department and to her room without multiple transfers. The end of the couch is lowered and the patient placed in the lithotomy position.

A special sterile pack is opened containing all of the items listed in Appendix 1. Sterile gloves are donned by the physician and drapes are placed over the patient's perineum and legs. The foot of the couch is also covered with a sterile drape. The entire technique from this point forward is done in a sterile fashion. A sterile speculum is emplaced and the cervix is examined. A metal skin clip, used as a radiographic marker, is clipped onto the cervix at either the 2:00 or 10:00 o'clock position. A Sims sound is then passed through the external cervical os and the uterine cavity is sounded for depth. This is usually done without the need for counter traction; however, if traction is needed a single toothed tenaculum is used. The sound is left in position and a ring forcep is slid along the sound to the external os and clamped to mark the depth of the uterine cavity. The two items are then removed together. The adjustable cervical collar of the Ridings' tandem is set so that the intrauterine portion of the tandem is slightly shorter than the sounded depth (Figure 1). There are two curves of Ridings' tandem available and the more appropriate one is used. The more steeply curved tandem is preferred to reduce rectal irradiation; however, in cases where the uterus lies posterior or has some degree of retroflexion or retroversion the straighter of the two tandems is used.

Following the insertion of the tandem the speculum is removed. The Fletcher "after loading" ovoids are disassembled and passed one at a time into the proper lateral fornix (Figure 2). The handles are then reassembled and spread as widely as can be comfortably tolerated. In those patients with larger vaginal vaults, plastic sleeves for the ovoids may be used; however, we have not found them necessary. Overly aggressive spreading of the ovoids is to be avoided because it is uncomfortable and might cause pressure necrosis of the vaginal vault. We usually spread the ovoids to the point of moderate discomfort and then relax them slightly. At this point a Foley catheter is put into the bladder and inflated with 5 cc. of "Hypaque."

Next the vaginal vault is packed with "Furacin" gauze. The packing is by far the most demanding part of the application for both the physician and the patient. The pa-

Appendix 1

TRAY FOR INTRACAVITARY RADIATION THERAPY APPLICATIONS

1. 1 each—Schroeder Utering Tenaculum forceps, 9″
2. 1 each—Foerster Sponge forceps, 9½″ cvd.
3. 1 each—Sims Sound
4. 1 each—Graves vaginal speculum, small
5. 1 each—Graves vaginal speculum, medium
6. 10 each—Wachtenfeld skin clips
7. 6 each—4 X 4's
8. 1 each—Suture scissors, S&S or S&B
9. 2 each—Foley catheter clamp
10. 2 each—O.B. towels
11. 1 each—12″ tissue forcep with teeth
12. 2 each—¾″ ribbon retractors
13. 1 each—Screwdriver
14. 1 each—Uterine Packing Forceps

WRAP SEPARATE

15. 1 each—Jackson Vaginal retractor, small
16. 1 each—Jackson Vaginal retractor, medium
17. 1 each—Jackson Vaginal retractor, large

PLACE TOWEL ON TRAY AND LAY INSTRUMENTS AS NEATLY AS POSSIBLE, LENGTHWISE ON TRAY. PLACE TOWELS ON TOP OF THESE. DOUBLE WRAP IN SPW'S.

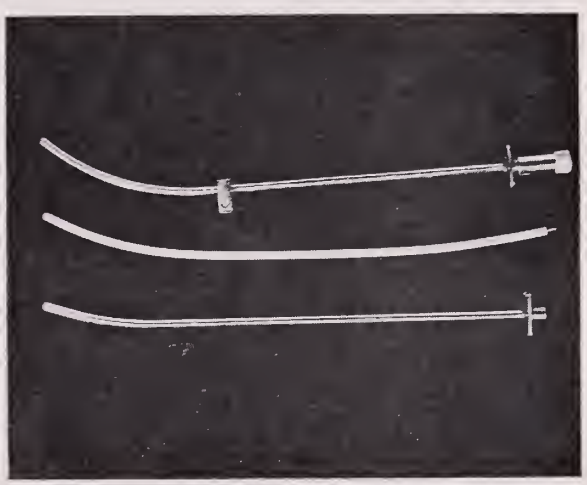


Figure 1. Two curvatures of Ridings' tandem with plastic insert for "after loading" radioactive material.



Figure 2. Set of Fletcher Ovoids with inserts for "after loading" radioactive material.

tient must be continually encouraged to relax the legs and lower the pelvis in order to allow proper packing. The physician must be patient and gentle to obtain the most cooperation and to attain the best possible geometric relationships for the application. For packing purposes we use malleable blade retractors bent to fit the individual patient and 10 inch forceps to pass the packing material.

A small amount of material is packed anteriorly between the ovoids on top of the tandem to prevent the posterior packing from forcing the tandem above the ovoids. An effort is made to pack completely against the cervix and to press the rectum as far away from the ovoids as possible. It is to be noted that it is not necessary to force packing under the ends of the ovoids themselves; this is difficult and quite uncomfortable for many patients and can lead to abrasions of the vaginal mucosa. The reader is advised to refer to page 453 of Fletcher's book, "Textbook of Radiotherapy," regarding cases in which special packing in front or in back of the ovoids is of advantage. In the Fletcher ovoids there is a special lead shield which attenuates radiation in the direction of the rectum and the bladder. This has proven to be quite satisfactory in Doctor Fletcher's hands with the use of radium. With our use of cesium we find that the rectum and bladder are shielded by essentially one-half value layer of shielding material. The lack of posterior and anterior ovoid packing is undoubtedly one of the reasons that packing is done satisfactorily without general anesthesia. Following completion of the packing, the entire application is observed for proper alignment and relationships between the butt of the tandem and the handle of the ovoids. In our packing the butt of the tandem lies posterior to the cross-bar of the handles of the ovoids in nearly all cases.

A small amount of thin barium or Hypaque is now injected into the rectum with a bulb syringe and a five dosimeter lithium fluoride flexible rectal dose monitor is put in place. A dummy load is placed in the Ridings' tandem. The dummy consists of the regular Ridings' after loading plastic tube which contains four steel nails, each exactly 2 cm in length. The tips and butts of these metal nails will serve as the location of sources for the computerized dosimetry runs.

The patient is then taken down from the lithotomy position and placed in a supine position. She is then wheeled to the X-ray Department on the treatment table where stereoscopic AP films of the pelvis are obtained for localization of the sources for the computerized dosimetry. In addition, a simple AP and across-the-table lateral films are made for preliminary check as to relative positions of bladder (demonstrated by Hypaque in the Foley), rectum (shown by the rectal dosimeters and rectal barium), and the applicators. The patient is then returned to her room and put into bed.

After review of the films a decision is made regarding the loading and the after loads prepared. A common load is 15-10-10 milligrams radium equivalent in the tandem and 15 in each ovoid. Upon the patient's return to the ward, orders are written which include radiation precautions (see Appendix 2), and strict bed rest, although the head may be raised to 30 degrees and the patient may lie on her side. The catheter is attached to straight drainage.

The following morning an AP film of the pelvis is made at the bedside. This radiograph is used to assure that the elements of the application have not changed their relative positions overnight. Also the lithium fluoride rectal dosimeter is removed and read to give the dosimetry at five points

within the rectum. The computer run is then made and evaluated.

All in all, we have found this technique to be quite well accepted and useful in the vast majority of our patients. Although somewhat uncomfortable, it has been used on women who are in their eighties. We have found that this technique requires a minimum of the physician's time away from the department. It is actually performed in the examining room and requires only 20-30 minutes of the physician's time. In addition, it saves the patient a considerable amount of time in the hospital, in that she has the application in place within two hours of the time of admission, rather than being admitted one day and going to the operating room the next. It eliminates the cost and physiologic stress of general anesthesia as well as the inherent dangers. In nearly all of our cases, two or more of these applications are performed. We have not had a patient who was unwilling to have the second application without general anesthesia. In addition, if examination of the film reveals the application is unsatisfactory in any detail, it is no problem to bring the patient back down to the department, unpack, reposition the application and repack it. This has been done on a few occasions with considerable improvement in the geometry of the application.

The radiation delivered to the therapist by this technique is markedly less than that from the usual techniques of applying a loaded applicator. In tests run in this department, a complete "after loading" procedure delivers an average exposure of less than five mrem to the physician. □

6161 South Yale, Tulsa, Oklahoma 74136

T. J. Brickner, Jr., MD, was graduated from Washington University Medical School in 1958. Certified by the American Board of Radiology, Doctor Brickner is a member of the American College of Radiology, the American Society of Therapeutic Radiologists, the American Radium Society and the Radiological Society of North America. He is Secretary-Treasurer of the Northeastern Oklahoma Radiological Society.

Since his graduation from the University of Arkansas School of Medicine in 1960, George H. Kamp, MD, has been certified by the American Board of Radiology. Doctor Kamp is a member of the Alpha Omega Alpha, the American College of Radiology and the Radiologic Society of North America.

David S. Gooden, PhD, received his degree from the University of Missouri in 1970. He is now Director of Biomedical Physics, Engineering and Mathematics at The William K. Warren Foundation in Tulsa. Doctor Gooden is a member of the American Association of Physicists in Medicine, the Nuclear Medicine Society, the American Institute of Ultrasound in Medicine and the American Society of Therapeutic Radiologists.

Appendix 2

INSTRUCTIONS FOR WARD PERSONNEL HANDLING PATIENTS CONTAINING RADIOACTIVE SEALED SOURCES

ALL PERSONNEL ATTENDING THESE PATIENTS SHOULD TAKE THE FOLLOWING PRECAUTIONS:

1. All routine nursing procedures shall be carried out in a normal fashion. However, personnel shall not spend more time than is absolutely necessary at the immediate bedside.
2. Pregnant women shall not attend these patients.
3. Visitors over 18 years of age shall spend no more than one hour per day in the room, and should stay as far from the patient as is convenient. Persons under 18 years of age shall not be permitted. Visiting privileges are subject to modifications with the expressed consent of the physician.
4. Pregnant visitors shall not be permitted.
5. It is preferable for patients to have a separate room or to be roomed with other therapy patients. Any other room arrangement must be approved by the physician. After a particular room situation has been approved by the physician, no changes should be made without first consulting him.
6. A "Caution Radioactive Material" sign shall be used to distinguish these patients. (This sign should be placed on the front of the patient's chart, and either on the bed, or on the outer side of the door to the patients' room.)
7. Packing material shall not be disturbed.
8. If the sources become displaced, the physician shall be notified immediately of the condition.
9. As soon as possible after the patient arrives on the floor, the original sheet of the Radiation Therapy-Source record shall be placed in the patient's chart with all entries up to date.
10. Since the radioactivity is encapsulated and cannot enter the bloodstream, no contamination will result from these patients. That is, the urine, feces, blood, saliva, etc. are not radioactive and do **not** require any special handling.

If these procedures are followed, the radiation exposure to personnel, other patients, and visitors will be kept to a minimum and remain well within the permissible limits as established by the National Committee on Radiation Protection.

II. The Urological Problems in Space Flight

A. T. K. COCKETT, MD
A. P. ROBERTS, BA
W. ROSS ADEY, MD

Space flight beyond 14 days has produced significant physiological alterations. We report the urological problems encountered prior to and during the flight of Bonny, a space monkey. Solutions to these problems are detailed.

WEIGHTLESSNESS, a condition present in orbital space flight, leads to alterations in the basic physiological systems of the astronaut. The purpose of this report is to outline the important urological problems which have been observed or encountered.

A significant aspect of this paper will detail our experience as a co-investigator* in the NASA Biosatellite Program. We outfitted the subhuman primate, Bonny, with a special indwelling urinary catheter.

In 1962 we suggested the possibility that urolithiasis was a potential hazard posed by the environment of weightlessness.[1] We reviewed the etiologic factors of urinary calculus formation and emphasized the conditions in space which were similar to the causes of calculi in selected groups of patients. We also mentioned the study by Ward[2] who suggested that urinary stasis in space flight was a distinct possibility because of a possible decrease in the "urge to void" at zero gravity. We subsequently demonstrated a flattening or thinning[3] of the urinary bladder musculature and urothelium of rats exposed continuously to a simulated altitude of 18,000 feet for eight weeks. We believe that prolonged space flights beyond 50 days at an altitude of 27,000 (5 PSI) may also create problems in voiding.

*Principal investigator—W. Ross Adey, MD.

From the Division of Urology, University of Rochester School of Medicine and Space Biology Laboratory, U.C.L.A. School of Medicine.

This study was supported by National Aeronautic and Space Administration Contract Number 2-5700.

MATERIALS AND METHODS

1. Urinary Catheter Development. A silicone rubber urinary catheter was developed for use in the male monkeys. A malecot-winged tip catheter was selected to provide a wider lumen for drainage. A special silicone disc was created to be buried below the skin of the perineal urethrostomy for anchoring. The catheter had special exterior attachments to prevent kinking of the catheter line. A loop arrangement was interposed between the catheter and the collecting device to allow for the increased forces of launch and re-entry.

Specialized catheter care was instituted from the time of surgery. A closed system was employed. Urinary bacteriologic specimens were obtained on both flight and ground-based control animals. Penicillin G (long acting preparation) was injected into the animals prior to the commencement of flight or hardware testing.

Table 1

URINARY BACTERIOLOGY AT SPACE FLIGHT CENTER
PERIOD 6-13-69 to 7-9-69

P-624	446	467	470	589
NO GROWTH	NO GROWTH	NO GROWTH	NO GROWTH	NO GROWTH
			6/18 PROT. MIRAB.	
			6/20 PROT. MIRAB.	6/20 PROT. MIRAB.
			6/22 NO GROWTH	6/22 PROT. MIRAB.
			6/24 NO GROWTH	6/24 NO GROWTH
			6/26 NO GROWTH	
				6/30 NO GROWTH
				7/02 PROT. MIRAB.
				7/04 PROT. MIRAB.
			7/07 NO GROWTH	7/07 PROT. MIRAB.

Table I. Urinary bacteriology on five animals prepared at Cape Kennedy Launch Center. P-470 is the flight animal (Bonny).

2. Calcium in the urine was determined after collecting urine samples every six hours. In the case of Bonny, a system for inflight calcium analysis was developed by several other investigators and will be reported separately.

3. Fluid intake and output of all animals in the test were carefully measured. The diuresis noted in Bonny is mentioned in results. Pre-test weights were obtained before immobilization. The weights of each animal after flight were also noted.

4. Testicular biopsies were obtained before and after immobilization. We have previously described in detail these changes.[4, 5, 6] We will illustrate these changes only in the flight animal.

RESULTS

Figure 1 is a photograph of our 15 Fr silicone rubber, urinary catheter. This indwelling catheter was maintained in a monkey for 66 days. The urine was not infected; Penicillin G had been injected into the animal at the beginning of the test, and it was reinjected after 30 days. Results of urinary bacteriologic studies at the time of the countdown at Cape Kennedy are shown in Table I. Five animals were prepared at the time of the pre-launch procedures. Bonny, P-470, was selected in spite of a positive urine culture. *Proteus mirabilis* was eliminated from the urine before launch by the penicillin G treatment. When Bonny was recovered after 8½ days of space flight, the urine revealed no growth of bacteria. A trace of penicillin G was still present in the urine.

In Figure 2 the calcium excretion in three out of four ground-based controls is plotted (mean). The fourth animal had an abscess beneath his skull and was eventually sacrificed. The elevation in calcium is seen after immobilization. After 15 days the calcium

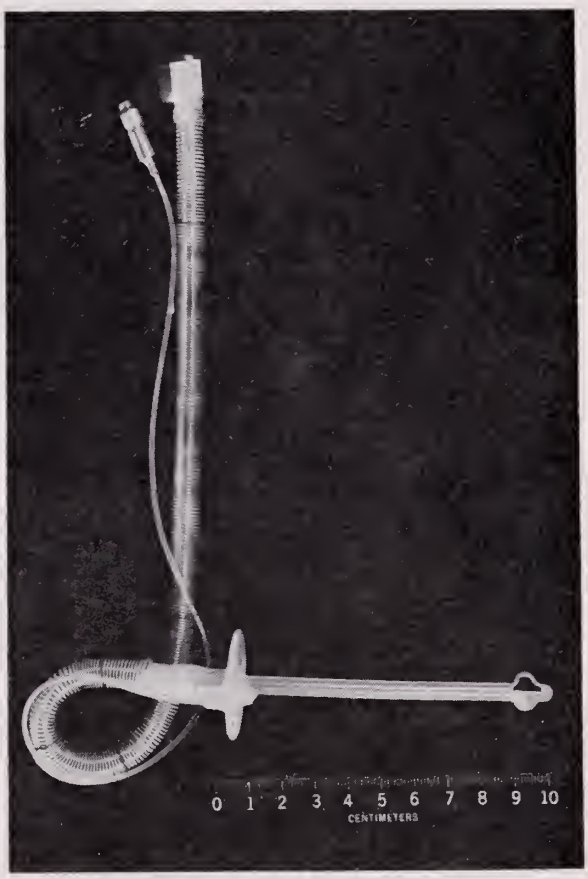


Figure 1. 15 Fr Silicone rubber indwelling urinary catheter.

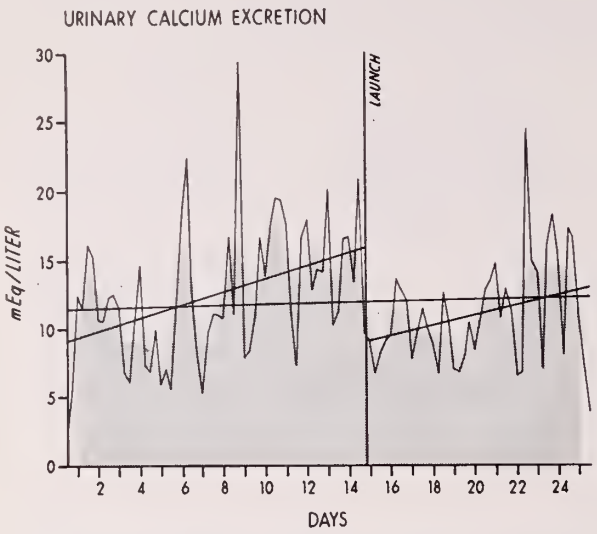


Figure 2. Calcium excretion in urine of 3 animals (average) held on the ground at Cape Kennedy.

levels are reduced to a lower level (7-8mE_2/liter). A gradual rise from days 15 to 25 is still evident in spite of day-night changes in capsule position. The calcium excretion is adjusted for urine volume in Figure 3. The data are plotted on a six hourly basis. A significant elevation in urinary calcium is seen throughout the immobilized period in these three animals.

Fluid intake and output of the flight animal Bonny is illustrated (Figure 4). The animal weighed 14 pounds prior to launch. A urinary diuresis is seen and reaches a

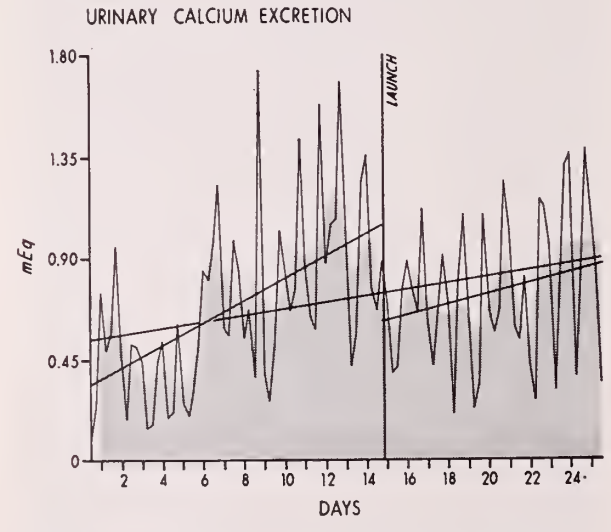


Figure 3. Calcium excretion adjusted for urine volume in 3 animals held on the ground. A gradual rise in calcium levels is seen.

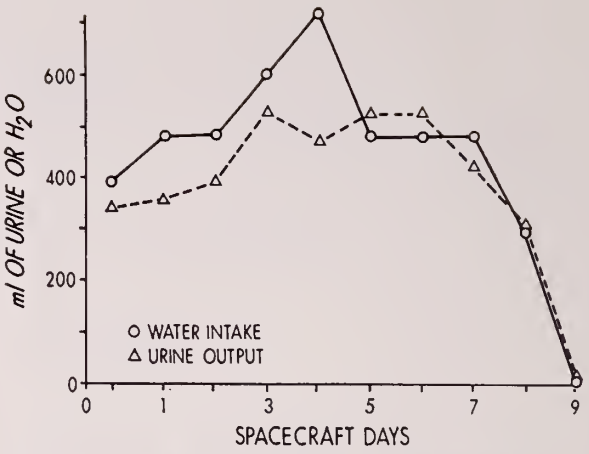


Figure 4. Intake and output of flight animal (Bonny) is illustrated. A urinary diuresis is seen. An output of 520 ml is seen on the third day of orbital flight.

maximum of 520 ml/24 hours during the third day of space flight. By reprogramming the water dispenser system, intake of water is increased.

Testicular biopsies reveal spermatogenic arrest in Bonny following his return (Figures 5A and 5B). The ground-based control animals also demonstrated these same changes after 14 days of couch restraint.

DISCUSSION

The silicone rubber catheter devised for use in our subhuman primates has been surgically implanted in pediatric cases. The 15 Fr catheter is non-reactive and has a wide lumen (3mm). In our animals the catheter was effective in transporting urine for periods up to 9½ weeks. Since subhuman primates excrete a urine of high pH, it was necessary to regulate urinary pH by developing a new diet high in casein.[7] This significant advance prevented sludging and clogging of the catheters by urinary sediment.

Penicillin G was injected intramuscularly (1.2 million units in each hip area) at the time of catheter implantation. Previous studies in our animal colony had demonstrated the presence of adequate urinary levels (50-75 mcg/ml) of the antibiotic after 15-17 days. We believe that the incorporation of a closed urinary system in combination with the antibiotic accounted for our success.

Immobilization has been previously demonstrated as a cause of urinary hypercalciuria. When the calcium excreted in three

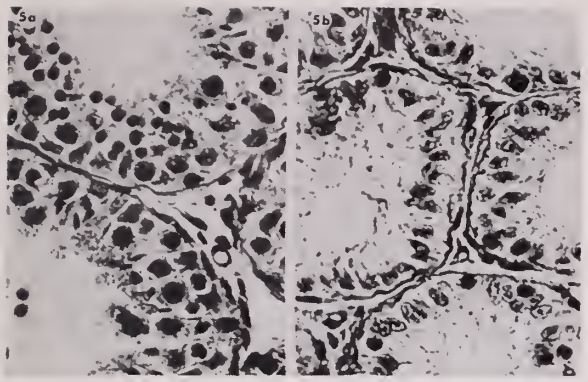


Figure 5A. Initial biopsy of testicle (P-470). 540x
Figure 5B. Biopsy of testicle (P-470) after 8½ days of flight and 13 days of immobilization. Spermatogenic arrest is seen.

of the four controls was adjusted for urine volume, a significant rise in urinary calcium was seen as the period of immobilization lengthened. The inflight urinary calcium information on Bonny is not available at present. We believe that the problem of bony decalcification and hypercalciuria is still a potential urological problem in space flight.

The diuresis sustained by the flight animal was somewhat surprising. Previous manned space flights had reported weight losses in the range of 4% of body weight. The combination of weightlessness and immobilization probably accounted for the demise of our animal. Approximately 20% of the animal's body weight was lost after 13 days of immobilization and 8½ days of space flight. A weight loss of this magnitude is sufficient to account for the death of the animal. Determinations were made of the insensible water loss and urine loss, thus allowing calculations of total fluid loss.

The initial objective of our testicular study involved a study of animal spermatozoa. This study was prompted by the report of abnormal spermatozoa in two Russian dogs that had orbited the earth for 22 days. Our study changed in its scope after the first few years because of the 13 day immobilization period before space flight. During the hardware tests conducted in 1966-1968, we discovered the alterations in spermatogenesis after 14 days of immobilization. We also learned in subsequent studies in our laboratory that these changes were reversible. Unfortunately FSH and ICSH gonadotrophic assays were not available to us. In future flights it would appear that these immunoassays along with determination of testosterone levels would be highly desirable. We have recently reported ultrastructural and histochemical changes in our biopsy specimens.[8] We believe that a wide-based approach should provide the diagnostic tools to assist in the unraveling of the etiologic factors in spermatogenic arrest.

Underway in our laboratory are the extraction of endogenous steroids from testicular slices. By employing labelled isotopes, e.g. C_{14} pregnenolone, it is possible to determine the major pathways of metabolism in this specialized tissue. We believe that this approach should also be beneficial and provide useful information in future flights.

SUMMARY

The urological problems encountered in the preparation of our flight, Biosatellite III, are mentioned. The methods and tech-

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Since his graduation from the University of Utah College of Medicine in 1954, A. T. K. Cockett, MD, has been certified by the American Board of Urology. He is presently Professor and Chairman of the Division of Urology at the University of Rochester School of Medicine. His medical affiliations include the Society of University Surgeons, the American College of Surgeons, the American Urological Association, the Northeastern Section of the American Urological Association and the Aerospace Medical Association.

A. P. Roberts, BA, is with the University of Rochester School of Medicine and Dentistry in Rochester, New York.

W. Ross Adey, MD, was graduated from the University of Adelaide, Australia in 1943. He is now Professor of Anatomy and Physiology at the University of California School of Medicine. Doctor Adey is a Fellow of the American Academy of Arts and Sciences, a member of the American Society of Neurological Surgeons, the American Physiology Society, the Aerospace Medical Association and the American Association of Anatomists. Doctor Adey is a member of the Space Science Panel, President's Science Advisory Committee.

niques used by our group to solve these problems are outlined.

Future flights involving animal experiments are possible. We believe that our techniques may have further use in other subhuman primate flights over the coming decade. □

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260 Crittendon Boulevard, Rochester, New York 14642

OSMA-OBA MEDICAL-LEGAL INSTITUTE

JULY 21st-22nd **ARROWHEAD STATE LODGE, LAKE EUFAULA**

Topics for this year:

Professional Corporations	The Physician Witness
Interprofessional Code	Medical Examiner's Law
Workmen's Compensation	Disease Reporting and Driver's License Revocation
Uniform Consumer Credit Code	Malpractice Arbitration

A cocktail party is planned for Friday afternoon to start about 5:00 p.m. This will give everyone time to go to Krebs for dinner. A short cocktail party and buffet dinner will be served Saturday evening. □

OSMA JOURNAL/special

"A Sentimental Journey"— Apologies to Laurence Sterne

WILLIAM S. MIDDLETON, MD

IF ONE MAY BE pardoned a literary allusion and be excused from any amorous implications, I can with all sincerity term mine a sentimental journey to convey to the graduates of the University of Oklahoma College of Medicine 1965 my hearty congratulations on their achievement of this objective. To me, this Class is truly a remarkable group of young men and women. Undoubtedly, I feel especially close to you for your part in affording me such a profitable and satisfying transition from pure administration to academic medicine (1963-4). With your participation I was granted the opportunity to study patients at the bedside from dawn to dark. It was a heavenly release from the exactions of official bureaucracy.

Osler said, "The man who is not fond of students and who does not suffer their foibles glady, misses the greatest zest in life." He should have known the Class of 1965! Reyes, whose ulcer I awaited momentarily; "doubting Thomas" Reed; Goree, whose weight I tried to control (by eating his French fried potatoes); Coker and Tucker, the gobs who saw the light; Bob Schacht, second generation exposed to my instruction, the content of whose black book I should like to know; Folsom, whose psychology began with silent prayer; Mrs. Stacy, Miss Pittston to me; Thornbrough, whose percussion was a personal challenge to me; Zahorsky who has never heard me profane; Capehart, whose reflex has not yet been recorded in the medical literature; Steve Haas, whose daughter Lisa won the Middletons' hearts; Barbee, whose son promises to be the White Hope in his father's judgment; Eakin of the Hollywood glasses; Meiring, whose swimming prowess is brought into the classroom; and so I could enumerate, with some personal annotations, the members of this unusual Class that means so much to me.

Zinsser said, "Learn from our pupils as we teach them. That is the only sound prophylaxis against the dodo-disease of middle age." Philosophers and sociologists have attempted to assign the basis for the election of teaching as a career. To me the gratification in the emergence of the alert, inquiring mind is one of life's greatest rewards.

In 1901 the drawing of lots for 13,000 parcels of land attracted 160,000 people to Oklahoma Territory. Among the hopeful who came to El Reno was Doctor Lewis Jef-

Being in substance the Commencement Address given at the University of Oklahoma School of Medicine, Norman, Oklahoma, June 13th, 1965.

ferson Moorman. A recent graduate of the University of Louisville College of Medicine, in a personal inventory he brought to Oklahoma "a medical diploma, a desire to see the West and an inferiority complex." After his original disappointment in the transaction at El Reno, Doctor Moorman sought a location for practice. The "Pioneer Doctor" recounts his remarkable career. To posterity in general, and to you, his professional progeny, in particular, I commend a careful study of this eminently human document. The chapters dealing with his Chickasha and Jet experiences are classics that afford a vivid picture of the trials and vicissitudes of medical practice under the primitive conditions of that period. The emergent visits to isolated homes in northers and under forbidding storms tried the mettle of man and beast. The Salt Fork of the Arkansas River constituted a recurring threat. His indomitable courage and faith prevailed and the rewards were not monetary. After six years Doctor Moorman sought a wider base and spent a period of professional rehabilitation in Vienna.

Of his subsequent career much has been written. Largely through his interest in tuberculosis, Doctor Moorman became a leader first in Oklahoma and then in the country at large. His "Tuberculosis and Genius" is a fascinating series of biographic essays on tuberculous notables. In some respects it might be termed "The Psychology of the Tuberculous Patient." His contribution to medical education is familiar to all of you; but it is to the altered picture of practice that I would here call your attention.

Gone is the "doctor on horseback" with his medical armamentarium in his saddle bags and the Plains physician in his buggy and buckboard. The modern graduate looks forward to practice rapidly gravitating toward the hospital. In the interest of time and effort, house and office practice are shrinking at a rapid rate. This is not an unmitigated blessing. Several questions have naturally arisen: Whose convenience? What expense? Like Topsy, the present pattern of hospital practice has just grown up. No one seems to have taken the pains to determine the soundness or stability of this growth. The family counselor remains the bulwark of our profession. With the complexity of modern medical science and practice, however, specialization is inevitable. Its form must be individually resolved and leaves the decision to you. The associate formula with common services and reception, laboratory and radiology has many advantages to recommend it. Among these may be cited the independence with interdependence among men of like background, ideals, and objectives. The scientific advances must be promptly assimilated in practice. An anxious public informed by science writers in many periodicals becomes restive in the gap between the bench and bedside. To segment one element of practice, therapeutics falters by reason of the lag in communication. In effect the laboratory and the special clinics are the producers. Pharmacists and the physicians are the purveyors. The patient is the consumer. Up to the present time through a series of media, information reaches the practicing physician and in turn the patient. Too frequently the primary source is the detail man representing a pharmaceutical house. Informed as he may be, he is not a physician, but the representative of a commercial organization. Medical schools must in the future continue their education of the profession throughout the active careers of its participants. By the same token adverse drug reactions do not promptly and regularly become common knowledge to medical practitioners. Several agencies involved are striving to remedy these patent faults. A consolidation and a simplification of drug information are long overdue. Furthermore a drug DEW line

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William S. Middleton, MD, graduated from the University of Pennsylvania School of Medicine in 1911. He is Emeritus Professor of Medicine at the University of Wisconsin Medical School.

Certified by the American Board of Internal Medicine, Doctor Middleton is a member of the American College of Physicians, the Royal College of Physicians, the Association of American Physicians, the Association of Physicians of Great Britain and Ireland and the American Clinical and Climatological Association.

should be established to give immediate warning to physicians of serious adverse reactions. In the minds of all of you now entering the practice of medicine, there must reside a most conservative frame of reference in the acceptance of new procedures and drugs. Significant as are the safeguards in the production and release of new medications, one must be ever alert for adverse reactions. Four hundred years B.C. Hippocrates said, "If you can do no good, at least do no harm." A corollary of this principle applies to your daily use of drugs. Should adverse symptoms arise that by any stretch of the imagination may be ascribed to its action, discontinue the drug and note the effect of this withdrawal on the symptoms or signs that have been observed. Many of the powerful drugs of recent origin are two edged swords. To further involve the intelligent use of these potent agents, such details as enzyme induction, genetics and drug interaction must be borne in mind.

On this happy but solemn occasion President Eliot's reflection comes to mind. He said, "Students bring so much to Harvard and take so little away." The thoughtful teacher has always on his heart the spirit of his students. Material as is much of our medical training, our patients are human, tried in mind and body by ills that warp or glorify that intangible but pervasive element that we term the spirit. Your foundation for a gratifying career in medical service has been laid under the supervision of a dedicated faculty, intramural and preceptorial. You will grow in strength and medical stature as you join your spiritual and intellectual talents. Admitted to the sanctity of the sickroom, you will appreciate your awesome responsibility to God and man. Here detached from the "leading strings" of professors, you will grow to your full stature, for only at the bedside can the true picture of disease be studied. Then, and then only, can you find real satisfaction in the delicate patient-physician relationship that glorifies medicine above all other human endeavors. Here you will find "satisfaction in the silence of intellectual accomplishment." (MacNider) Nor should you insulate yourself from society at large. In the greater social fabric, medicine in general and you in particular must take your place among the health arts; the captain, but not the whole team.

Members of the Class of 1965, my heartfelt wishes for your health and your success. May you reward your "opportunity with labor." (Mitchell) God bless you. □

MEDICAL-LEGAL INSTITUTE

JULY 21st-22nd **ARROWHEAD STATE LODGE, LAKE EUFAULA**

A two-day medical-legal institute of interest to both physicians and attorneys is being jointly sponsored by the OSMA and the Oklahoma Bar Association. Scheduled for the beautiful Arrowhead State Lodge on Lake Eufaula, the meeting will cover such topics as Professional Corporations, Workmen's Compensation, the Uniform Consumer Credit Code as it Applies to Professionals, Food and Drug Administration Rules and Regulations, Privileged Communications, and an Explanation of the New Medical Examiner's Law in Oklahoma.

A cocktail party is scheduled for Friday evening and a buffet dinner Saturday night.

The meeting has been planned by the joint Medical-Legal Relations Committee of the OSMA and OBA. Registration fee for the two-day meeting is $40 to cover the cost of course materials, the cocktail party Friday and one ticket to the dinner Saturday evening.

Advanced registration should be directed to the Oklahoma State Medical Association, Attention Ed Kelsay, 601 N. W. Expressway, Oklahoma City, Oklahoma 73118. □

HMO—Hope or Hoax?

FRANK A. RIDDICK, JR., MD

Date on costs, patient and physician satisfaction, quality of care in closed panel prepayment practices cast doubt on the role of the HMO as a panacea.

THE TITLE ASSIGNED for this talk is, "What Lies Ahead for the Practice of Medicine?", but insiders confided to me that my assignment would be to emphasize the private fee for service half of this panel on Group Prepayment Practice vs Private Fee for Service. One thing which medicine faces is a determined push by the Federal Government to make prepayment group medical care available through stimulating the formation of what they term Health Maintenance Organizations (HMO). The role assigned to prepayment groups in the various proposals for national health insurance varies from inclusion with mild toleration to vigorous espousal and provision of deterrents to fee for service practice.

HMO's

Until legislation is actually passed it will be impossible to describe an HMO with certainty. A general description is that it is a private or public corporation which provides health services to enrollees, either directly or through arrangements with others, on a per capita prepayment basis. It must provide enrollees with all the services reasonably required by a defined population to be maintained in good health. Minimum services must include emergency services, inpatient hospital and physician care, ambulatory physician care, and outpatient preventive medical services. It should have financial responsibility and the capacity to provide comprehensive health care services efficiently, effectively, and economically, and should have at least 10,000 enrollees. All proposals include some provision for peer review requirements for each HMO.[1, 2]

A variety of types of organizations conceivably could function as HMO's, including medical schools, community hospitals and their staff physicians, and Medical Society Foundations or some other entity receiving a fixed capitation payment, but paying the physicians on a fee for service basis. But it is clear that only an organization which possesses or is capable of readily integrating both professional and institutional services will be able to qualify. Existing prepayment group practices, especially Kaiser-Permanente, are usually cited as prototypes of the HMO, and data from these are given to support the claims of superiority of this approach.

The major reason advanced for favoring the HMO capitation approach is cost savings; the fee for service payment is viewed by some as a temptation to deliver excessive or unnecessary services. Other reputed advantages are more efficient use of manpower and facilities, improved medical care, and better distribution of health care to areas of need. A claim, indicated by the name chosen, Health Maintenance Organization, is that by receiving a lump sum each year for care, the organization will be stimulated to prevent illness in its enrollees as it will have to pay the costs of treating them when ill.

The Department of Health Education and Welfare has asked for 45 million dollars to

Ochsner Clinic and Ochsner Foundation Hospital, New Orleans, Louisiana 70121.

Presented as a portion of a Panel on Group Prepayment Practice vs Private Fee for Service at the Annual Meeting of Washington State Medical Association, September 22nd, 1971 in Seattle, Washington.

assist a number of HMO's. Pending this appropriation, they have diverted 16 million from other sources. It is estimated that the costs of establishing an HMO *de novo* run from 1¼ million for an urban HMO serving a general population to 2¼ million for an HMO for the urban poor, plus an additional 4 to 8 million in construction costs. The cost of a rural HMO is estimated at 3½ million dollars, including construction.[1] Lesser amounts are required for conversion of existing facilities. At present, some 60 HMO groups have been approved for funding, so that the program can hardly be considered experimental. The aim of the Department of Health Education and Welfare is to have an HMO available to 90% of the population by 1980.[3]

COSTS

The problem of rising costs of medical care is a matter of national concern. The nation's bill for health services was 67 billion dollars in 1970; the Federal Government paid 25% of the total, and state and local governments 12%. Inflation, affluence, delivery of a greater volume of services to a larger population, introduction of new and complex therapy and technology, all have contributed to the rise, but the most spectacular increase has been in hospital costs, which have skyrocketed to nearly 300% of their 1960 value. While unit costs for medical services have climbed in the past decade, the rate of rise is the same as that for other services measured in the consumer price index.[4]

To what extent does prepayment group practice cut costs and how are the savings brought about? Most studies indicate that the total cost to the individual is less when prepayment group practice plans are compared with other insurance coverage, largely by virtue of higher out of pocket expenses in the latter. Some studies do not agree. The total payment on behalf of Medicare recipients in two large prepayment groups, one on the West Coast, the other, the East Coast, was compared with the total payment on behalf of the other Medicare recipients who were not on the prepayment plan. Fewer dollars were expended for the West Coast group compared with other Medicare patients from that area but the reverse was true in the East.[5] The HEW white paper "Towards a Comprehensive Health Policy for the 1970s"[3] presents the data from the two divisions of the West Coast group practice, and ignores the data from the East Coast.

There is general agreement that the rate of hospitalization is less for members of prepayment groups than for holders of standard health insurance policies, even when age factors are considered.[6] The comparison is at times a bit unfair. When a plan which pays for both in-hospital and outpatient medical expenses is compared with one which pays only for services rendered in a hospital, it should surprise no one that the latter has the higher rate of hospitalization regardless of the mechanism of paying the doctor.[7] The patients will see to that.

It is difficult to be precise about how many fewer hospital days are spent by prepayment group members than non-group members. There is more variation from study to study and area to area than between the prepayment group and non-group patients in the same area.[6] Nonetheless, with fewer hospital days, we would expect costs to be less, since this reduces the most expensive component of medical care. The question is, are the cost savings related solely to a reduction in hospitalization rather than to prevention of disease by health maintenance? To what extent are less costly alternatives provided as opposed to the patient not receiving the service or seeking it outside the plan?

If prepayment group Y enrollees use 500 hospital days per 1,000 members per year and those with other forms of health insur-

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A 1954 graduate of Vanderbilt University School of Medicine, Frank A. Riddick, Jr., MD, has been certified by the American Board of Internal Medicine. He is now Clinical Associate Professor of Medicine at Tulane University School of Medicine. He is a Trustee of the American Society of Internal Medicine and an Alternate Delegate to the American Medical Association from Louisiana. He is a member of the American College of Physicians, the Endocrine Society and the American Diabetes Association.

ance use 1,000 hospital days per 1,000 members per year, it does not necessarily mean that 500 excessive days were used by the non-group patients. It may mean that there was preselection in the group; it may mean that group members only got half the hospital time they needed. It could mean that both the prepayment group and non-group doctors deviated from optimal utilization by 250 patient days per thousand, in which case the costs measured in dollars would be less for the prepayment group, but the costs in illness and suffering greater.

We will come to the question of use of services outside the prepayment group under the heading of patient satisfaction, but it is of importance under costs. Unless the volume and costs of out of plan services are added in, there will be significant distortion in cost figures.

Does elimination of fee for service contain costs? Both England and Sweden have experienced increases in medical costs somewhat greater than has the United States. The capitation rate at Kaiser-Permanente has increased yearly (except one) since 1957 in Southern California, and (except four) in Northern California.[8]

I have had the privilege to visit Kaiser-Permanente on two occasions in the past four years. I am impressed with the managerial efficiency which applies the big business approach to delivery of health care, backed with a wealth of data analyzed on an actuarial basis. Much as Mr. Kaiser's engineers calculate what is needed to build a dam—how many tons of concrete, how much steel, how many bulldozers—so do the experts in the health plan calculate how many hospital beds, offices, pediatricians, nurses aides will be required to deliver what is needed to a given population. They thrive on a stable base of employed middle class subscribers, whose premiums are largely paid by the employer. The rates are set up and quoted much as car insurance or homeowners policies are. That is, they set up a budget, deciding how many cents per member per month are required to meet the expenses of running each part of the system, medical benefits, hospital benefits, administrative costs, etc. In so doing, they do the same thing for which hospitals, Blue Cross, and physicians are criticized and castigated. They build in a five percent item on hospitalization to cover research, education, and community service. They have a four percent required profit for all capital items they own. In addition, they have a required minimum of 15 cents per member per month to finance further expansion. If their anticipated needs exceed the current premium, they hike the premium. There is great incentive to stay within the budget, as unexpended funds are split between the hospitals and the medical groups. This bit of lagniappe has amounted to $9,000 per man for the past few years. It is of interest that their estimate of needs continues to rise, yet they continue to have the surplus noted and do not pass savings on to subscribers.

In the Northern California region the income to the group per member is $170 this year. This is not the premium, which varies with the number of members in the family. What does the member get for his $170 each year? It averages out to be half a day in the hospital (value approximately $50), 5 lab tests, 3.6 visits to the doctor, and 0.8 x-rays. This isn't cheap, and on a fee for service basis would average out at $28 per doctor visit. These data do not lend themselves to a decision as to whether costs are controlled by people not coming to the doctor or by the doctor preventing disease and keeping them healthy, but I tend to lean toward the former.

If holding down medical costs is going to be of paramount importance, the least expensive health care system is a judicious mixture of Christian Science and euthanasia.

QUALITY OF CARE

There are few studies which bear on the quality of care delivered by prepayment group practice. One which is cited in the white paper, "Towards a Comprehensive Health Policy for the 1970's" reports that the death rate of elderly persons is less under care of an HMO than with "traditional" medical practice.[3] However, the original study involved elderly welfare recipients in the pre-Medicare days. One group was enrolled in a prepayment group practice; the other group continued to receive care in mu-

nicipal clinics, with house calls made by another set of physicians from a panel maintained by the Welfare Department, and any hospital care delivered by a still different group of hospital staff physicians.[9] To term this type of medical care as traditional is misleading. Further, the small difference (annual death rates 7.8 per 100 vs 8.8 per 100) and the fact that the reported difference was observed only for the year and a half *after* the study ended raise doubts as to the usefulness of the data.

Studies in the New York City area do show a difference in prematurity rates and perinatal mortality rates to enrollees for obstetrical care in a group prepayment plan compared to the general obstetrical population in New York City, with the group prepayment plan having the more favorable rates.[10] These differences are partially, but not entirely, abolished when group prepayment deliveries are compared with those attended by private physicians in New York City.[11] The reasons for the differences are not clear, but a much larger percentage of deliveries were attended by board certified obstetricians in the prepayment group, and it is not clear that patients delivered by private physicians had all received prenatal care from these physicians.

The fact of the matter is that we have no good data concerning management of comparable groups of patients under the prepayment group plan compared with care in the offices of private physicians. Outcome data as well as data on the medical process will be required. It will not be sufficient to compare medical care in the prepayment group against a group not receiving care at all.

I do not believe that the private practicing physician views the patient as a sheep to be shorn of dollars under the guise of delivering medical care. Both patient and physician are aware of cost factors in delivering medical care. The decision to investigate a given problem or not has a significant economic component, even when undertaken to reassure the patient or the physician. If we grant that fee for service has economic stimulus to investigate or treat the marginal or unsettled problem, then prepayment group practice has the economic stimulus to ignore them. In which case is the patient best served? Further, if there are a few physicians, who through poor practice habits or cupidity, generously overtreat, overhospitalize, and overtest, to their economic gain, what will they do when it is to their monetary advantage to undertreat, ignore, and not investigate indications of possible disease?

I was told by the director of a newly formed prepayment group that he had informed his surgeon, facetiously I hope, that his pay would be docked for every "cold" appendix removed. My response was a warning to prepare for the highest rate of ruptured appendiceal abscesses in town.

The economic pressures for the prepayment group to stay within a budget can be intense. It is undoubtedly cheaper to dispense coronary vasodilators to the 45-year-old who presents with angina pectoris than to refer him to a medical center and pay for coronary cinearteriography and perhaps a saphenous vein aortocoronary bypass operation. What happens towards the end of the year, when the funds for services outside the plan are running low, and such referrals must be paid from the kitty for salaries?

Prepayment plans point with some pride to a reduced rate of elective surgery, especially on the female reproductive system. It is perfectly possible to manage menorrhagia and dysmenorrhea in a 38-year-old woman with iron and analgesics over the next ten years, and it is cheaper than the hysterectomy which would more effectively relieve her symptoms.

PHYSICIAN SATISFACTION

Although the number of physicians in group practice has increased dramatically to nearly 20% of non-federal physicians in patient care,[12] the number of prepayment groups have grown at a relatively slow rate and serve less than five percent of the population. Eighty-five of the 6,341 group practices in the United States provide a significant amount of care on a prepaid basis. The current push toward formation of HMO's indicates that the Department of Health Education and Welfare believes that prepayment groups will not be established without economic stimulation.

It is a mistake to assume that the average physician is familiar only with fee for service practice. Most physicians have served in the armed forces, and many have worked in the Medical Department of the Veterans Administration in medical school and postgraduate training programs. Such exposure has not created a stampede into prepayment group practice.

How satisfied are the physicians in group practice? Like the East Germans, they can vote with their feet. Last year 12½% of the non-partners and five percent of the partners left Kaiser-Permanente. In the Permanente groups sixty percent of the physicians are under 45, and the median age is 42. Half have been with the program less than five years, and 75% less than ten years.

A study of the attitudes of physicians in one prepayment group practice indicated that ¼ to ⅓ of the physicians perceived an adverse effect on the physician-patient relationship, the delivery of quality care, and on their own professional standing, related to practice within a group prepayment practice.[13]

PATIENT SATISFACTION

One measure of patient satisfaction is the number who stay with the plan. A recent survey indicated that 87.4% of members said they would renew with the Kaiser Foundation Health Plan, down from 94% a decade earlier.[8]

Another measure is the number who seek services outside the plan. In 1968, Kaiser members covered by Medicare received out of plan services which amounted to 18% of the capitation premium in Northern California, and 16% in Southern California. Outside physicians are used for 37% of surgical operations in the Health Insurance Plan of New York, 14% of all paid physicians' services and 33% of home visits in Kaiser-Permanente, and 23% of physicians' and dentists' services in the Labor Health Institute of St. Louis.[6] Over a three-year period, 39% of the members of the Community Health Association of Detroit used physicians outside the plan, and the most recent sample of Kaiser enrollees reported that 44% have seen physicians outside the plan. Thirty-five percent of the members of one prepaid health plan, and 38% of another prepaid group did not consider the plan physician to be their "regular" or "family" physician. Studies indicate that the individual who has a regular physician is less likely to choose a prepayment group, and if he does, is less likely to be satisfied with the group and more likely to seek services outside the group.[6]

The Kaiser group has wisely insisted that their program be offered only as an alternate to other health plans. This insures that their members are there because they want to be. To an outsider, it appears that they are set up to deliver competently and efficiently the necessary services to a group. They determine which services are necessary, however, and one is forced to wonder how well the general American public will accept just what is necessary instead of what they are accustomed to in the way of personal service and reassurance. A public which supports the health food industry, visits chiropractors, and ingested several tons of vitamin C to ward off colds last year is not precisely attuned to accepting medical care in scientifically measured dollops or the therapeutic nihilism to which prepayment disposes. Dr. Sidney Garfield's "worried well"[14] may accept being shunted off to a machine or a team of allied health workers, but I don't think that the "worried well" and worried patients with stabilized asymptomatic disease, and the worried patients with an essentially untreatable condition in my practice will.

EFFICIENT PRACTICE ORGANIZATION

Appropriate delegation to well supervised allied health workers, efficient organization to assure proper use of hospital facilities, continuous availability of services, and development of proper referral patterns are not exclusive attributes of prepayment group practice; they exist in any well organized fee-for-services group practice. They may also be found in the community of independently practicing physicians which develops in a geographic area, usually in the vicinity of a hospital. This has been referred to as the "group without walls."

FEE FOR SERVICE PRACTICE

The payment of a fee for a service rendered remains a reasonable, honorable, and effective way of paying for medical services, as it is for other services and goods. It places the responsibility on the recipient of services and gives recompense to the man who does the work. It serves as an incentive for the physician to be available at odd hours and inconvenient times, to use his time efficiently and effectively, and to satisfy the patient. It needs no apology. Mike Halberstam has noted, "I don't mind piecework payment—most professionals are paid this way and so is Renata Tibaldi."[15]

The fee serves as a deterrent to seeking medical attention frivolously but, with appropriate insurance coverage, is no barrier to effective medical care. The consumer has greater freedom. If he is dissatisfied, he can get another opinion and seek care elsewhere, which may be difficult or unnecessarily costly if he has signed up to receive all his care from one particular organization. Importantly, it keeps the emphasis on provision of medical care, rather than rewarding the non-provider.

Under fee for service practice, the effective arms of the hospital medical staff, the Medical Audit Committee and the Utilization Committee, and the Medical Society Peer Review Committee confer safeguards of maintaining quality and assuring that monies are expended for indicated and appropriate care. Medical societies and hospital medical staffs must meet this challenge of involvement in effective quality assessment.

MAINTAINING HEALTH?

It is difficult to escape the conclusion that the major factor kindling such interest in prepayment group practice, is the desire of government to contain costs and to have a budgetable quantum of medical care negotiated. This is beclouded by the concept that what is purchased is health, or at least that health will be maintained through organizing and delivering medical services in a particular way. Evidence suggests that cost savings of prepayment group practices are effected by a reduced rate of hospitalization rather than by keeping people healthy. The automated multiphasic screening unit at Kaiser-Permanente was designed as an investigative tool in delivering medical care. It is used in part as a physician substitute. However, only about five percent of the Kaiser Health Plan members in the Northern California area could use it for an annual check-up if they desired.[16] It would take until 1991 to run all their members through the screening unit once.

It is not clear that the experience of prepayment groups offer a nationally applicable solution to problems of delivering medical services, that they apply to unselected patient groups or can overcome geographic restraints in areas of sparse population, or that they will be universally acceptable to patients. It is unwise to give large financial subsidies to establish prepayment group practice until these answers are obtained through appropriate study. □

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News From The Oklahoma State Department of Health

A knowledge of rubella immunity status in the woman of child bearing age is an important component in the provision of good perinatal health care. Between 80 and 90 percent of women in the child bearing years are immune to rubella as a result of past infection. But for that 10 to 20 percent who do not possess protective antibody, rubella can be a serious problem.

Immunization campaigns against rubella begun early in 1970 have already greatly reduced the number of reported cases of rubella. As of early April in 1970, over five hundred cases of rubella had been reported to the State Department of Health. This number dropped to less than 40 in 1971, and to less than ten cases by the same date in 1972. The risk of congenital rubella has decreased at approximately the same rate. But for the young pregnant woman exposed to rubella in early gestation and unsure of her rubella immunity status, the anxiety suffered has *not* decreased. The problems faced by the physician caring for such a patient are equally difficult. Routine serologic testing of young women prior to the child bearing years would be one method to provide baseline immunity information to simplify handling of potential exposure situations.

The most valuable serologic tool used in rubella immunity testing is the rubella hemagglutination inhibition (HI) technique. HI antibodies rise rapidly in rubella infection. The titer increase is often detectable before the rash subsides, and has usually peaked at a titer of approximately 1:1024 by ten days after onset of the exanthem. The HI titer is generally very stable remaining at a level of 1:64 or so for many years. A titer of at least 1:20 is considered protective.

We believe that every woman between the ages of 15 and 45 should know her rubella immunity status. If not immune she can be immunized providing she is not pregnant nor will become so within two months of immunization. If immunization is contraindicated, knowledge of immunity status can provide the means for rational handling of the rubella exposed pregnant woman. □

COMMUNICABLE DISEASES IN OKLAHOMA FOR MARCH, 1972

Disease	March, 1972	March, 1971	Feb. 1972	Total to Date 1972	Total to Date 1971
Amebiasis	4	4	3	8	17
Brucellosis	—	—	—	—	—
Chickenpox	12	27	39	88	70
Encephalitis, infect.	—	3	2	2	7
Gonorrhea	691	587	856	2306	1662
Hepatitis, infect. & serum	54	70	66	162	175
Leptospirosis	1	—	—	1	—
Malaria	1	14	—	1	35
Meningococcal infections	2	2	1	3	4
Meningitis, aseptic	2	3	3	6	10
Mumps	18	63	40	89	117
Rabies in animals	41	63	14	63	118
Rheumatic fever	—	1	7	8	5
Rocky Mt. spotted fever	—	—	—	1	1
Rubella	—	9	—	2	32
Rubella, congenital syn.	—	—	—	—	—
Rubeola	—	171	—	1	577
Salmonellosis	9	6	7	19	40
Shigellosis	9	2	4	14	26
Syphilis	65	118	125	270	336
Tetanus	—	—	—	—	—
Tuberculosis, new active	25	36	21	62	77
Tularemia	1	—	—	1	—
Typhoid fever	—	—	—	—	—
Whooping cough	1	2	3	5	6



STANLEY R. McCAMPBELL, MD

Meet the President

On May 20th Stanley R. McCampbell, MD, became the Oklahoma State Medical Association's 67th President. He replaced Lucien M. Pascucci, MD, Tulsa.

A cardiologist in Oklahoma City, Doctor McCampbell is a 1952 graduate of Vanderbilt Medical School. He served his internship in the Second Cornell Medical Division of Bellevue Hospital in New York City.

His residency in internal medicine and cardiology was taken at Bellevue, New York Hospital, and in the Postgraduate Medical School, London, England.

While claiming Tennessee as his state of birth, Doctor McCampbell chose to enter private practice in Oklahoma in early 1958. He is an instructor in the Department of Medicine and Preventive Medicine at the University of Oklahoma School of Medicine.

Doctor McCampbell and his wife, Joan, have four children, two daughters, Sody, 17, and Kelly, 11, and two sons, Robert, 14, and Jimmy, 12.

Having been active in organized medicine for several years, Doctor McCampbell has served on several councils and committees for the OSMA and is a Past-President of the Oklahoma County Medical Society.

A tennis enthusiast, he has served as the President of the American Medical Tennis Association. □

Peer Review Foundation Activated By OSMA

On December 12th, 1971, the House of Delegates of the OSMA authorized the creation of a new foundation dedicated to providing peer review for any organization, insurance company, or government health program, needing such. The foundation has now been activated and all members of the OSMA have been invited to join.

The creation of the foundation was to give the OSMA the upper hand in the event that a national system of peer review was created by Congress. There is a bill pending before the United States Senate Finance Committee at this time which would establish such a system that would require physician peer review groups to review each and every claim filed against the government for health care services wherever rendered.

Although the OSMA House of Delegates disapproves this impending infringement on medical practice, it was the unanimous consensus of the delegates that organized medicine should manage such a program if one is necessary. The implementation of the Oklahoma Foundation for Peer Review will put the association in a favored position to be the administrative agency for a peer review program.

On March 15th all members of the association were notified of the implementation and asked to sign an agreement card giving the foundation the exclusive right to provide peer review services for the physician-signer. As of mid-April well over one-half of the OSMA members had signed and returned the card.

The bylaws of the new foundation require that its board of directors shall consist of 15 participating members, and the President, President-Elect and Chairman of the Board of Trustees of the OSMA, who shall be ex-officio members with a voice, but without the right to vote. Of the 12 members, four shall be from Oklahoma County, three from Tulsa County, and the remaining five from other counties throughout the state. The board members must be engaged in the active practice of medicine at all times while serving on the board.

The board members will supervise the activities of the foundation and will not necessarily be on the review committees. Any such committees that are established will be broadly representative on both a geographic and a specialty basis.

The initial board of directors is made up of Arnold G. Nelson, MD, James B. Eskridge, III, MD, Scott Hendren, MD, and Art Schmidt, MD, all of Oklahoma City. The three Tulsa members are Roger V. Haglund, MD, C. S. Lewis, Jr., MD, and Rollie E. Rhodes, Jr., MD. The five remaining members are Hillard E. Denyer, MD, Bartlesville; Howard B. Keith, MD, Shattuck; Fred D. Switzer, MD, McAlester; Maurice C. Gephardt, MD, Muskogee; and William M. Leebron, MD, Elk City.

Any physician wishing to join the foundation should sign the agreement card and return it to the Foundation For Peer Review in care of the OSMA in Oklahoma City. In the event that the card has been misplaced, the following statement may be typed out and signed by the physician:

"I, the undersigned, hereby authorize the Oklahoma Foundation for Peer Review the exclusive right to provide a peer review service on my behalf as may be required under existing governmental or private health insurance programs, or as may be required by future federal legislation." □

Another Proposal For National Health Insurance

A modified version of the American Hospital Associations Ameriplan emerged in Congress in early April as a new national proposal for financing and delivering health care. Avoiding the use of the phrase "national health insurance," the new proposal refers to a "national health care" plan.

Embodying certain basic features contained in the shelved Ameriplan proposal, the revised plan is known officially as the "National Health Care Services Reorganization and Financing Act." It was introduced by Representative Al Ullman (D-Oregon), second ranking member of the House Ways and Means Committee.

The author characterizes the bill as a mechanism that is "truly workable and not just theoretically appealing." It calls for a development of a system of health care corporations, known as HCCs, to provide health care in designated geographic areas. There would be at least one HCC in every state. The corporations would be non-profit, community based organizations run by hospitals, physicians or other providers.

The plan would mandate employer contributions toward health insurance coverage for their employees, with employers paying 75 percent of premium costs. In addition an incentive to encourage individuals to join an HCC would be provided, with the federal government paying 10 percent of their insurance premiums.

The measure would institute national health care coverage by steps taking place over a four-year period. The first step would consolidate all federal health programs within the Health Education and Welfare Department and would combine Medicare Parts A and B without co-payment or deductible and would extend Medicare to low-income persons. The programs would be coordinated by a "Office of Health Affairs."

State Health Commissioners would review applications for HCC franchises and would control rates charged by HCCs, non-affiliated providers and private insurance carriers. The commissioners also would devise methods for providing insurance coverage for the poor and near poor. Estimated federal cost of the plan would be $16 billion annually, primarily from general revenues.

During the second step of the four-year program catastrophic health insurance benefits would be extended to all persons. The third step would require comprehensive health care benefits broader than those during the initial steps. □

The Other "AMA" Cooperates With Health Agencies

Members of the other AMA, American Motorcycle Association, are cooperating with four agencies in an effort to inform motorcyclists, parents of cyclists and officials of the inherent health hazards involved in cycle riding. Working in conjunction with the Oklahoma State Health Department, the Department of Public Safety, the Oklahoma County Medical Society, and the OSMA, the motorcyclists have launched a statewide information campaign.

OSMA President Lucien Pascucci, MD, said, "With the increase of motorcycle riding by people from all walks of life and in all age and economic brackets, we feel that it is imperative that a stand be taken with regard to the hazards involved in cycle riding."

"Although cycles provide an outlet from the hectic pace of today's world, a means of entertainment for young and old alike, it is impossible to deny the dangers involved even to the safety conscious rider," he said.

An automobile provides a certain amount of driver protection because of its enclosed body, wheel base, and degree of control. The cycle with its power, two wheel construction, balance factor and lack of enclosure around the driver offers little protection to its occupant in the event of a collision.

Doctor John A. Blaschke, MD, President of the Oklahoma County Medical Society said, "Nearly every sport available to man involves hazards. This is perhaps part of the fun of mastering the sport. Few sports, however, expose the participant to a potential impact with hard pavement or fixed objects at speeds up to 80 miles an hour."

"Even the best riders are subject to changing road and weather conditions, poor judgment on the part of automobile drivers, and sudden changes in wind direction. It is the combination of all of these which must lead concerned physicians and parents to exercise extreme restraint in providing cycles for their own young people. Not that motorcycles are a bad thing, but they must continually be respected in much the same way as a loaded shotgun," Blaschke continued.

There were 60 deaths and 1,535 injuries attributed to motorcycle accidents in 1971 according to statistics from the Oklahoma Department of Public Safety.

Doctor Leroy Carpenter, MD, Commissioner of the State Health Department, noted that deaths resulting from motorcycle accidents kill more people every year than most of the dread diseases totaled. In 1970 the number of deaths in Oklahoma attributed to typhoid, polio, measles, whooping cough, smallpox, diphtheria, scarlet fever, rheumatic fever, meningitis, encephalitis and infectious hepatitis was only 45. Fifty-three deaths resulted from motorcycle accidents in that same year.

The President of the Capitol City Riders, an Oklahoma City Motorcycle Club, said "Learning to ride is only part of cycle riding, because defensive driving techniques and inherents to traffic laws is an absolute must in order to be a safe cyclist. Those who ride motorcycles should remember that their machines leave no margin for error, as in the case of an automobile. Also, because of the small size of a cycle, a motorist may not see the rider and turn into him."

The motorcycle safety campaign will consist of using the mass media to dispense safety information. □



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New Hospital Named For Mark R. Everett, MD

The University of Oklahoma Board of Regents recently voted to name the new University Hospital the Mark R. Everett Tower in honor of the dean emeritus of the College of Medicine.

Doctor Everett, 72, retired as dean of the College of Medicine and director of the OU Medical Center (now the Health Sciences Center) in 1964.

The Mark R. Everett Tower, nearing completion in the Health Sciences Center in Oklahoma City, is the first 214-bed unit of the new University Hospital. The $11,791,000 structure is tentatively scheduled for occupancy in September.

Doctor Everett was dean and director at the time the new hospital was planned and the state bond issue which provided the local funds to build it was passed. □

MD Named To OU Regents

Bob G. Mitchell, MD, Sallisaw, has been named as a member of the University of Oklahoma Board of Regents to succeed Horace K. Calvert of Oklahoma City.

Governor David Hall, in announcing the appointment, described Doctor Mitchell as ". . . a country doctor with a general practice in Sequoyah County. He shares this administration's determination to deliver quality health care to the rural areas of Oklahoma and our commitment to the best education possible for Oklahoma youth."

A 1956 graduate of the University of Oklahoma Medical School, Doctor Mitchell has been named to a seven year term on the Board of Regents. He attended Northeastern State College and Oklahoma State University prior to entering medical school. He practiced medicine in Henryetta 18 months and then opened his current practice in Sallisaw.

Doctor and Mrs. Mitchell have four children, Angela, 18, a sophomore at the University of Oklahoma; Robert, 16, Marcinda, 13, and Kelly, 11. □

DEATHS

DAVY L. GARRETT, MD

1888-1972

Davy L. Garrett, MD, a Tulsa surgeon since 1923, died on March 4th, 1972. Born in Gainesville, Texas, Doctor Garrett graduated from the Atlanta College of Physicians and Surgeons, now Emory University School of Medicine, in 1910. He practiced in Altus, Oklahoma, from 1912 until moving to Tulsa.

Doctor Garrett was a member of the American Board of Surgery, the American College of Surgery and the Southeast Surgical Congress. He was presented a Fifty Year Pin by the OSMA in 1960. In 1961, the Auxiliary to the Tulsa County Medical Society honored Doctor Garrett by naming him "Doctor of the Year."

BEDFORD F. PETERSON, MD

1910-1972

Bedford F. Peterson, MD, Superintendent of Eastern State Hospital, Vinita, died in his home March 1st, 1972. A native of Jonesboro, Arkansas, Doctor Peterson was graduated from the University of Tennessee College of Medicine in 1933. He was with the Western State Hospital in Bolivar, Tennessee, and the Eastern State Hospital in Knoxville, Tennessee, before coming to the Eastern State Hospital in Vinita, Oklahoma, in 1964.

Doctor Peterson was a member of the American Psychiatric Association, the Southern Psychiatric Association and the Oklahoma District Branch of the American Psychiatric Association.

ROBERT W. GEYER, JR., MD

1927-1972

Robert W. Geyer, Jr., MD, an Oklahoma City radiologist, died April 13th, 1972. Born in Little Rock, Arkansas, in 1927, Doctor Geyer was graduated from the University of Arkansas School of Medicine in 1957. He came to Oklahoma City in 1961 where he was Instructor in the Department of Radiology at the University of Oklahoma Health Sciences Center. A year later he entered private practice.

J. M. McMILLAN, MD

1904-1972

A well-known Vinita physician, J. M. McMillan, MD, died in Tulsa on March 3rd, 1972. Born in Atlee, Arkansas, Doctor McMillan was graduated from the University of Oklahoma Health Sciences Center in 1933. He moved to Vinita in 1938 where he joined the staff of Eastern State Hospital. In 1942 he began private practice, establishing an office in Vinita. He retired in 1970.

Last year Doctor McMillan was presented an Honorary-Life Membership in the Oklahoma State Medical Association. He had been a member of the American Psychiatric Society and the Tulsa branch of the American Academy of Family Physicians. □

Medical-Legal Institute Set For July

A Medical-Legal Institute of interest to all Oklahoma physicians and attorneys is being jointly sponsored by the OSMA and the Oklahoma Bar Association. The institute will be held at Oklahoma's beautiful Arrowhead Lodge on Lake Eufaula, July 21st-22nd.

The two-day meeting will cover such topics as professional corporations, workmen's compensation, the new medical examiner's law, privileged communications, and malpractice arbitration.

A registration fee of $35 per person is being charged to cover the cost of all course materials, a cocktail party on Friday evening, and cocktails and a buffet dinner on Saturday evening. Tickets for the buffet for wives may be purchased for only $4.00.

The Saturday evening buffet menu will include four entrees: barbequed beef spareribs, fried chicken, assorted fish consisting of fish sticks, ocean perch, portions of fish squares, and roast beef. A variety of vegetables and assorted wines will be served to tingle the tastebuds. The dessert cart at Arrowhead is covered with such goodies as peach and cherry cobbler, chocolate pudding, assorted pies, petits' fours, whipped cream parfait, and ice cream on request.

The following is a brief listing of the topics to be given on the two days:

Friday—Professional Corporations, The New Interprofessional Code, Workmen's Compensation (Percent of Disability Versus Percent of Physical Impairment), Uniform Consumer Credit Code, and a demonstration of an examination and cross examination of a physician-witness. In addition, talks will be given on the Limitations of X-ray, Limitations of EEGs, and an orthopedic examination demonstration.

Saturday's program will begin with an explanation of the Medical Examiner's Law, A discussion of the disease reporting now required for driver's license revocation, and a section on privileged communications. An explanation of the Food and Drug Administration Rules and Regulations and how they apply to the practice of medicine and become involved in the practice of law will take part of the afternoon with a final section given on malpractice arbitration.

A cocktail party is scheduled for early Friday evening so that those who wish may go to Krebs, Oklahoma, for dinner in one of its outstanding restaurants . . . Pete's Place, Isle of Capri, or Gia Como's. □

Placement Service Seeks Information

One of the many functions of the OSMA is to serve as a "physician placement agency" for doctors wishing to enter practice in the state. In order to better fill this function, the association needs information.

All association members are urged to report practice opportunities to the placement agency . . . practice possibilities for both general and specialists. The information should be sent to OSMA Physician Placement Service, 601 N. W. Expressway, Oklahoma City, Oklahoma 73118.

In particular, the service needs specific recommendations regarding placement of specialists. Information for location of general practitioners is also requested. When writing the service please specify the type of physician needed and give some general information about the practice opportunity . . . i.e., size of the community, office space availability, hospital availability, the possibility of a partnership or office sharing agreement, etc.

Throughout the year the association receives a number of inquiries from physicians seeking new places to practice. The information requested above will enable the association to match up the opportunity with the inquiring physician.

The service is also available to Oklahoma physicians seeking to move from one community to another. □

Doctor Thompson Receives Award



C. THOMAS THOMPSON, MD

C. Thomas Thompson, MD, Tulsa surgeon, has been awarded the national "Trauma Achievement Award" for exceptionally meritorious service as a member of a regional committee on trauma.

Doctor Thompson, a member of the board of Saint Francis Hospital and Chairman of the Oklahoma Chapter of the American College of Surgeons Committee on Trauma for the past three years, received his award at the 50th anniversary dinner of the ASC Committee on Trauma in Charleston, South Carolina. This is the first year that this national award has been given.

The Oklahoma Committee on Trauma conducted one of the first emergency medical training classes for ambulance personnel at Saint Francis Hospital early in 1970, produced an Oklahoma Directory of Emergency Services and Facilities, and was the first in the country to administer the National Emergency Training-Ambulance Registry test. A project to train the majority of presently employed ambulance personnel in Oklahoma and to raise them to the level of the qualified Emergency Medical Technician (Ambulance) has been given the highest priority by the Oklahoma Regional Medical Program for federal funding for a three year period. □

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Telephone JA 8-7755

Innovations in County Society Meetings

If your county medical society is having difficulty getting proper attendance at its monthly meetings, you might consider the approach taken by Oklahoma's Okmulgee County Medical Society.

The society has a dinner meeting, and just one peek at the menu is enough to convince almost anybody that it's a good place to be on the second Tuesday of any given month. On April 11th the committee met in the Okmulgee Memorial Hospital with the following menu:

Chilled creamed vichyssoise
Poulet flambe Ile de France on rice
Green beans a la Nicoise
Romaine salad with artichoke hearts
French rolls and butter
Chocolate souffle or souffle a la Grand Marnier
Coffee

Of course, with such a menu, a good wine is necessary . . . Chablis 1969.

It is reported that attendance is excellent and that appetites were outstanding! □

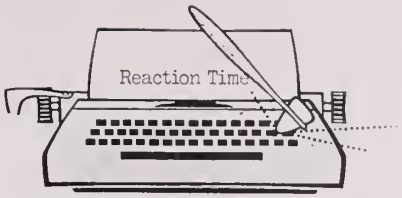
Physicians Paid $2 Million

In March of 1972, Oklahoma physicians were paid $2,059,200 through the Department of Institutions, Social and Rehabilitative Services. This represented medical help to 49,000 individuals.

The figure is somewhat misleading since it also includes the amount of deductibles and co-insurance payments for individuals over the age of 65 on Welfare and Medicare. For an indigent person over 65 DISRS pays their Medicare payments.

The above payments, which represent 25.7 percent, were physicians payments for Title XVIII, Part B, Medicare, or $528,500.

The figures were released by L. E. Rader, Director of Institutions, Social and Rehabilitative Services, in a letter to Lucien M. Pascucci, MD, President of the Oklahoma State Medical Association. □



Charles R. Block, MD
The Wichita Clinic
3244 East Douglas
Wichita, Kansas 67208
Dear Doctor Block:

I have enjoyed reading your article "The Treatment of Urinary Tract Infections in Children" in the Oklahoma State Medical Association Journal; however, I was somewhat distressed by two statements relating to carbenicillin:

> "The dosage schedule in children is not well known. The current expense of the drug is prohibitive."

The dosage schedule in children (50-300 mgm/kg/day) is well known and is clearly indicated in the package insert of Geopen. Those recommendations were based on a wide clinical experience dealing with several hundreds of pediatric patients.

The cost of therapy with carbenicillin is admittedly high when treating such conditions as septicemia, particularly in adults. Here, maximum recommended dosage of 30 to 40 grams per day is often used. However, in urinary tract infections, generally the lower limit of dosing is recommended because of exceedingly high serum and urine levels of carbenicillin achieved with such a regimen. Under those conditions, a child weighing 66 lbs. or 30 kgms. would require 3 grams of carbenicillin per diem. This is sold to a hospital pharmacy for approximately $8.00 when carbenicillin is purchased in quantities. I think that this certainly is not prohibitive when you consider the added safety one has when using a semisynthetic penicillin instead of an aminoglycoside.

Sincerely yours,
ANTHONY K. KNIRSCH,
DVM, MD
Associate Director
PFIZER PHARMACEUTICALS

AKK/dlo
cc: Oklahoma State Medical Association Journal

Book Reviews

THE PEDIATRIC NURSE PRACTITIONER. By F. J. deCastro, MD, MPH, FAAP, FAPHA, Assistant Professor of Pediatrics and Community Medicine, St. Louis University, Director of Ambulatory Pediatric Services, Cardinal Glennon Memorial Hospital for Children, St. Louis, Missouri, and Ursula T. Rolfe, BA, MD, Assistant Professor of Pediatrics and Community Medicine, Associate Director of Ambulatory Pediatric Services, St. Louis University. 1st Edition, Cloth, 154 pp. St. Louis 1972, The C. V. Mosby Company. $6.50.

Although there are numerous programs presently set up in the United States to train Pediatric Nurse Practitioners, Doctors deCastro and Rolfe have written the first text for these new health care professionals with a uniform, concise approach to ambulatory pediatrics. The book is intended as a guide for graduates from the programs as well as an outline for nurses in physicians' offices who have never received formal training as pediatric nurse practitioners, but are functioning as such. There are three major parts to the book: 1) Health Appraisal, 2) Clinical Problems, and 3) Social Problems.

The topics reviewed under each of these headings include an excellent discussion of how to take an "informative pediatric history" and how to get the most out of physical exam as a diagnostic tool. There is an attempt to simplify the discussion on the developmental appraisal and a check sheet insert of the Denver Developmental Screening Test is included. However, the chapter (6) leaves the reader with a superficial appreciation of the enormous amount of time these types of evaluations really entail.

The discussions of the Clinical Problems, in general, tend to be too brief, with the exception of the chapter on infectious diseases, which is concise, and well presented as to pertinence, pertaining to the Pediatric Nurse Practitioner's role.

The authors, in attempting to be complete in scope, have sacrificed

depth. Discussions on toxicity and doses of commonly used analgesics, how to "sponge" a child with increased temperatures, or how to approach a conference with parents in an effort to elicit which, if any, emotional problems are present in the home, are examples of topics which are woefully ignored.

The book might better serve as a guide for specialists in the field who are involved in teaching Pediatric Nurse Practitioners, but I do not feel a recent graduate from a Pediatric Nurse Practitioner Program would find this volume a useful resource guide to use in practice because it is not explicit or detailed enough in many areas of management.—*Jo Ann Wine, MD*

THE CARE OF THE GERIATRIC PATIENT. By E. V. Cowdry, PhD, ScD and F. U. Steinberg, MD. Fourth edition, cloth, 441 pp. with 52 illustrations. St. Louis: The C. V. Mosby Company, 1971. $21.00.

Although the senior editor of this book is not a physician, he is a distinguished scientist and authority on the physiology of aging. This is the fourth revision of his book which brings together a wide variety of information which should prove helpful to the physician dealing with the geriatric patient. He has recruited 53 authorities to contribute chapters for this book.

The book is divided into four sections, covering medical care, surgical care, nervous and mental care and delivery of care. Much of the first two sections read like abbreviated textbooks of medicine and surgery. Although the chapters in these sections are oriented toward problems which are more common and, in some cases, specific for aged persons, one might question the wisdom of or need for dealing with geriatric problems differently or separately from those dealt with by specialists in internal medicine and surgery. Two chapters on the nutritional and sexual aspects of aging are particularly noteworthy and provide excellent discussions on topics that merit attention.

The third section covers the neurological, psychiatric and psychological problems encountered in the aging patient. The discussions on the adaptation of the geriatric patient in the community indicate the considerable concern the authors experience about the complex problems encountered in this area. This is carried over into the next section on delivery of care where much useful information is provided on hospital, nursing, home and rehabilitative care along with points on selection of a nursing home. In the chapter on hospitalization, a tabulated summary of the coverage provided by Medicare is nicely presented.

This book then deals not only with the broad medical and surgical problems encountered by the aged patient but also with psychosocial and economic problems and provides information on delivery of care at all levels from the home to the hospital. For the general physician who deals with a large number of older patients, the book provides a wealth of concise information that would be hard to find covered elsewhere.—*Robert D. Lindeman, MD*

SYNOPSIS OF PEDIATRICS. By James G. Hughes, BA, MD, Professor of Pediatrics and Chairman of the Department of Pediatrics, University of Tennessee College of Medicine. 3rd edition. Hardback, 1141 pp. with 88 illustrations. St. Louis: The C. V. Mosby Company, 1971. $14.50.

This third edition, emerging only four years since the last edition, exemplifies what Doctor Hughes and the Pediatric staff at the University of Tennessee College of Medicine wish to provide for "students" of pediatrics at all levels of training and practice. The book is a "synopsis" but relatively thorough review of general pediatrics which is concisely written, and has kept abreast of the many new advances in pediatric medicine. This synopsis provides a clear and precise overview of virtually all topics of interest to the pediatric student and practitioner. This is accomplished in a practical manner with attention to many basic concepts and mechanisms of disease.

The book is well indexed and organized. There are many graphs, figures and tables, which enable the reader to easily understand the accompanying text of the particular topic. The chapters on "Autosomal Abnormalities and Genetic Counseling" are particularly good in this regard.

This book offers a practical approach to the workup and evaluation of patients presenting with many various clinical problems, particularly those which are complicated and may become more so if a rational plan is not followed such as offered in this synopsis.

Of particular interest to pediatric medical students and housestaff officers, is the chapter of pediatric surgery. This condenses into a simple, straightforward manner many of the common pediatric surgical problems encountered in children.

This well-written synopsis serves as an adequate introductory reference, but should be supplemented by reference to more detailed texts.—*John Steumky, MD*

PSYCHOLOGY OF EMOTION: SELF DISCIPLINE BY CONSCIOUS EMOTIONAL CONTINUENCE. By John M. Dorsey, MD, University Professor and Chairman, Department of Psychiatry, Wayne State University, Detroit, Michigan. First edition. Cloth, 213 pp. Detroit: Center for Health Education, 1971. $6.95.

It is generally stated that emotion and intellect are separate aspects of man's "living experience." In this book the author takes issue with such a statement and offers his personal philosophy of emotion. Doctor Dorsey states that the nature of mind is, in fact, emotion. Consequently, if one is to truly possess wisdom or intellect he can do so only through first possessing a conscious awareness of emotion. He must live all of his emotions and all of his experiences and consciously know they are his. If he is able to reach this level of feeling he will achieve unity within himself and hence, a true "oneness with life." The author acknowledges that accepting responsi-

bility for all of one's emotional experience is indeed difficult. He also feels, however, that all problems of mankind are directly traceable to undeveloped emotional control in the individual. If one accepts this premise, the necessity for achieving "conscious emotional continence" is obvious. The author's style of writing is, at best, ponderous but his thoughts are highly stimulating if the reader possesses the "intellectual continuence" to pursue them.—*David A. Vore, PhD*

PATHOBIOLOGY: AN INTRODUCTION. Edited by Jeff Minckler. MD, PhD, Associate Clinical Professor of Pathology, University of Colorado Medical Center, Denver, Colorado; Harold B. Anstall, MD, Professor of Clinical Pathology, University of Utah College of Medicine, Salt Lake City, Utah; and Tate M. Minckler, MD, Chief, Department of Medical Automation, Presbyterian Medical Center, Denver, Colorado. First edition, cloth, 522 pp. Saint Louis: The C. V. Mosby Company, 1971. $12.50.

The editors of this book have attempted something badly needed and long overdue, an approach to general pathology which would put in context the revolution undergone by pathology in the last 20 years. Further, they have directed the book specifically to non-pathologist physicians and to members of allied medical fields oriented to medical therapy.

This extremely ambitious endeavor has scored one spectacular success. No other monograph documents so vividly the enormous spectrum of contemporary pathology. No other monograph gives a non-pathologist a pathologist's insight into the varied approach to disease which underlies modern medical care. An abridged, partial list of topics includes: cellular pathology, molecular biology and clinical chemistry, genetic diseases, embryologic disorders, aging, toxins, chemotherapeutic mechanisms, iatrogenic diseases, immunopathology, physical agents of disease, irradiation and chemical agents of disease, deficiency disorders, ecologic pathology, forensic pathology, laboratory quality control, and computerization. Standard topics such as anatomic pathology and infectious diseases are, of course, represented in their contemporary form. The great benefit to be derived from this book is a grasp of the breadth of pathology *circa* 1971. To those who intellectually equate the words pathologist and autopsy, *Pathobiology* is mandatory reading.

Members of the "allied health professions" may find this introduction to general pathology less useful for two reasons. First, the layout and scope of the text both tacitly assume an understanding of pathology as it existed prior to 1950. Hence, some of the points of emphasis lack context. Second, some of the authors, including one of the editors, have missed their target audience almost completely. For example, in the fourth paragraph of the "Transport" chapter, one encounters, "Phospholipids behaving as zwitterions make up about half of the phospholipid present [in cell membranes]." The space occupied by the chapter on "Chemotherapeutic Mechanisms" is largely absorbed by no less than 36 organic chemical structural diagrams of various drugs, all completely uninterpretable without previous knowledge of organic chemistry. Hopefully, in any second edition, the authors will all emulate the lucid prose of senior editor Jeff Minckler.

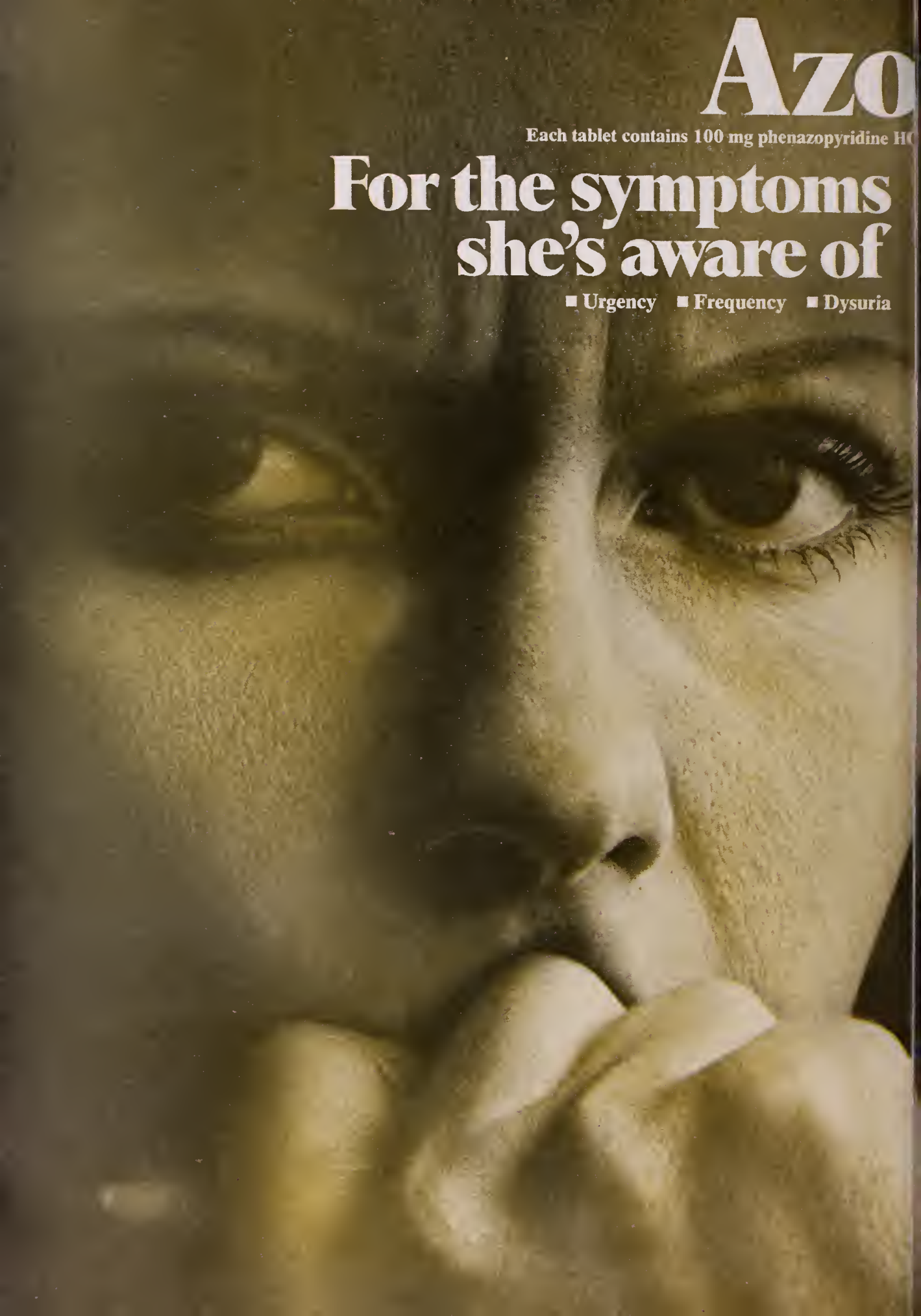
Pathobiology is specifically recommended to non-pathologist physicians as a splendid orientation in contemporary pathology. It would be of very considerable interest to anyone in medical care administration with responsibilities for laboratory medicine. Non-physicians would be well advised to examine the book carefully prior to purchase to assure that the presentation of the topics does not overwhelm their scientific background.—*Perry A. Lambird, MD*

A HISTORY OF POLIOMYELITIS. By John R. Paul. New Haven and London: Yale University Press. 486 pp.

The late John Paul began his research on poliomyelitis in 1931 and went on to become the leader of the Yale Poliomyelitis Study Unit and one of the authorities on this disease. He has provided us a detailed, penetrating, but very illuminating and readable story of one of medicine's most exciting chapters. The book is divided into 42 chapters. In the first ten rather brief chapters, the history of the disease from ancient times to the more recent epidemics is traced. Excellent accounts are given of the early epidemiologic studies of Caverly, Wickman and Frost. The contributions of Lansteiner, Simon Flexner and other important developments in the history of poliomyelitis are described. Paul writes interestingly about his own work, but perhaps too modestly about its value. He played a major role in identifying the disease called poliomyelitis as a relatively rare complication of an exceediingly common or usually silent infection of the intestinal tract. He had a large share in clearing up the confusion about human immunity. Eventually poliomyelitis was brought under control by means of two kinds of vaccine—one made of live and one of inactivated poliovirus. The last five chapters of the book deal with their development and the intense competition between their respective proponents. His portrayals of the many individuals and other organizations with whom he worked during his life are fascinating. His incisive description of his relationship to leading investigators in the fields of poliomyelitis such as John Enders, Albert Sabin, Dorothy Horstmann and others makes for fascinating reading.

From Carl Landsteiner's discovery of the virus in 1908 to the development by Albert Sabin of the live attenuated vaccine in 1960, the last 32 chapters read like a master detective story with successes and setbacks, personalities, organization and governments all playing a well analyzed role.

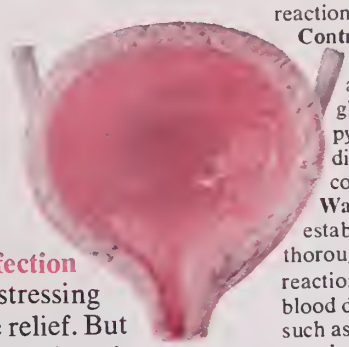
This book is a valuable, historical contribution which will be of interest to the many who have been or are concerned with poliomyelitis and other infectious diseases.—*Harris D. Riley, Jr., MD* □


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For the symptoms she's aware of
■ Urgency ■ Frequency ■ Dysuria

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nd 0.5 Gm sulfamethoxazole.

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Urgency, frequency, dysuria—these are the distressing symptoms of cystitis for which she wants immediate relief. But rapid control of the infection is equally important to both patient and physician. This is the situation that demands dual-action Azo Gantanol: the analgesic action of Azo (phenazopyridine HCl) for rapid relief of pain, the antibacterial action of Gantanol® (sulfamethoxazole) to control the bladder infection.

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basic therapy

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Nutley, N.J. 07110

Before prescribing, please consult complete product information, a summary of which follows:

Indications: In adults, urinary tract infections complicated by pain (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli, Klebsiella-Aerobacter, Staphylococcus aureus, Proteus mirabilis,* and, less frequently, *Proteus vulgaris*) in the absence of obstructive uropathy or foreign bodies. *Important Note:* Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response. Add aminobenzoic acid to culture media for patients already taking sulfonamides. Increasing frequency of resistant organisms currently is a limitation of the usefulness of antibacterial agents. Blood levels should be measured in patients receiving sulfonamides for serious infections, since there may be wide variations with identical doses; 12 to 15 mg/100 ml is considered optimal for serious infections; 20 mg/100 ml should be the maximum total sulfonamide level, as adverse reactions occur more frequently above this level.

Contraindications: Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period. Contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with gastrointestinal disturbances, because of phenazopyridine HCl component.

Warnings: Safe use in pregnancy has not been established, and teratogenicity potential has not been thoroughly investigated. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported; clinical signs such as sore throat, fever, pallor, purpura or jaundice may be early indications of serious blood disorders. Complete blood counts and urinalysis with careful microscopic examination should be performed frequently during sulfonamide therapy.

Precautions: Use with caution in patients with impaired renal or hepatic function, severe allergy, bronchial asthma and in glucose-6-phosphate dehydrogenase-deficient individuals. In the latter, hemolysis, a frequently dose-related reaction, may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias:* agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia; *allergic reactions:* erythema multiforme (Stevens-Johnson syndrome), skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis; *gastrointestinal reactions:* nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis; *C.N.S. reactions:* headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia; and *miscellaneous reactions:* drug fever, chills, toxic nephrosis with oliguria and anuria, polyarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide and thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

Dosage: Usual adult dosage for acute, painful phase of urinary tract infection is 4 tablets initially, then 2 tablets morning and evening. If pain persists beyond seven days, causes other than infection should be sought. After relief has been obtained, continued treatment with Gantanol (sulfamethoxazole) may be considered.

NOTE: Patients should be told that the orange-red dye (phenazopyridine HCl) will color the urine soon after ingestion.

How Supplied: Tablets, each containing 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl, bottles of 100 and 500.

Miscellaneous Advertisements

WOULD LIKE TO PURCHASE two used gynecological examining tables with matching cabinets, stools, trash cans, etc. Would pay one-half of original price if they are in fair condition. Might be interested in other used equipment. Contact Key S, The Journal, Oklahoma State Medical Association, 601 N.W. Expressway, Oklahoma City 73118.

INTERNIST NEEDED in one of Oklahoma's fastest growing communities — Claremore. Seventy-five bed community hospital with plans to double in the next two years. Set your own schedule in this fine community. Office space available July 1st in new clinic. Mail inquiries to Drawer B, Claremore, Oklahoma 74017.

VETERANS ADMINISTRATION Regional Office in Muskogee, Oklahoma, has one vacancy for the position of Medical Officer (Disability Evaluation). Duties consist of evaluating medical aspects of claims for disability compensation. Salary range: $20,627 to $25,388 per annum; 8 a.m. to 4:30 p.m., Monday through Friday, nine paid holidays, annual leave, sick leave, and other excellent fringe benefits. For complete information call or write: Mr. F. M. Emerson, Jr., Personnel Officer, Veterans Administration Regional Office, Second and Court Streets, Muskogee, Oklahoma 74401, Telephone 918 683-3111, Extension 202.

FREEDOM, HAPPINESS, AND CHALLENGE!!! Since you are reading this, you are probably dissatisfied with long hours, no free time for family or hobbies, cost of living, and/or your local community problems. We are looking for a skilled general practitioner under 55 to join our 40-bed JCAH-accredited hospital and outpatient clinic. Manhattan is a town of 30,000 friendly people located in the beautiful, rolling Flint Hills with two large lakes, cultural attractions you wouldn't believe, recreation and sporting opportunities aplenty, regular 8-5, minimum call three to four nights per month, salary $24,000, one-month paid vacation. But more important, we offer freedom and happiness in a healthy and beautiful environment. It only costs ten cents for more information since we can't tell you everything in this ad. R. E. Sinclair, MD, University Hospital, Kansas State University, Manhattan, Kansas 66502.

PHYSICIANS WANTED. Planning to build multi-suite Professional Mall in Weatherford, Oklahoma, a friendly fast growing college city; will build to suit. Need Two MDs. Write T. J. Toma, DDS, Box 310, Weatherford 73096.

SURGEON LOOKING FOR LOCATION. Graduate of Paris Medical School; U.S. internship and residency; licensed in New York and Pennsylvania. Board eligible. Contact A. Sergie, MD, 113 Duncan Street, Dublin, Georgia 31021.

OPPORTUNITY FOR GENERAL PRACTICE (with specialty interest if desired) in El Reno, a city of 15,000 only thirty minutes west of Oklahoma City. Established clinic of three doctors, adjacent to modern community hospital desires one or two associates for active group practice. Attractive salary and partnership opportunity. Let us show you a good deal. Contact Canadian Valley Clinic, 2001 Park View, El Reno, Oklahoma 73036 or call collect 405 262-2114, F. W. Hollingsworth, MD.

DICTIONARIES — WEBSTER, Library size, 1971 edition, brand new, still in box. Cost new: $45.00. Will sell for $15.00. Deduct ten percent on orders of six or more. Mail to North American Liquidators, 1450 Niagara Falls Boulevard, Department KK-166, Tonawanda, New York 14150. C.O.D. orders enclose $1.00 good will deposit. Pay balance plus C.O.D. shipping on delivery. Be satisfied on inspection or return within ten days for full refund. No dealers, each volume specifically stamped not for resale. Please add $1.25 postage and handling. New York State residents add applicable sales tax.

FOR SALE: Used X-ray machine, Profexray. Also other items for doctor's clinic. Call or write Billings Chamber of Commerce, c/o Aubrey Tipton, Billings, Oklahoma 74630. Phone 725-3424. □

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Pinworm therapy is often a family affair





Contraindications: History of hypersensitivity to thiabendazole.
Warnings: If hypersensitivity reactions occur, drug should be discontinued immediately and not resumed. Rarely, erythema multiforme has been associated with thiabendazole therapy; in severe cases (Stevens-Johnson syndrome), fatalities have occurred. Because CNS side effects may occur quite frequently, activities requiring mental alertness should be avoided. Safe use in pregnancy or lactation has not been established.
Precautions: Ideally, supportive therapy is indicated for anemic, dehydrated, or malnourished patients prior to initiation of anthelmintic therapy. In presence of hepatic or renal dysfunction, patients should be carefully monitored.
Adverse Reactions: Most frequently encountered are anorexia, nausea, vomiting, and dizziness. Less frequently, diarrhea, epigastric distress, pruritus, weariness, drowsiness, giddiness, and headache have occurred. Rarely, tinnitus, hyperirritability, numbness, abnormal sensation in eyes, blurring of vision, xanthopsia; hypotension, collapse; enuresis; transient rise in cephalin flocculation and SGOT; perianal rash, cholestasis and parenchymal liver damage; hyperglycemia; transient leukopenia; malodor of the urine, crystalluria, hematuria; appearance of live Ascaris in the mouth and nose. Hypersensitivity reactions

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include: fever, facial flush, chills, conjunctival injection, angioedema, anaphylaxis, skin rashes, erythema multiforme (including Stevens-Johnson syndrome), and lymphadenopathy.
Supplied: Chewable tablets, containing 500 mg thiabendazole, in boxes of 36, strip packaged, individually foil wrapped; Suspension, containing 500 mg thiabendazole per 5 cc, in bottles of 120 cc.

For more detailed information, consult your MSD representative or see the Direction Circular. Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa. 19486

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addendum

INDICATION | DOSAGE SCHEDULE

MINTEZOL® (Thiabendazole, MSD) has demonstrated effectiveness against a broad spectrum of nematode infestations, whether encountered singly or in combination. Dosages are weight related; therefore, a weight-dose chart is included in the Direction Circular for your convenience when writing a prescription. MINTEZOL should be given after meals if possible.

INDICATIONS	DOSAGE (1st Day)	ADDITIONAL REGIMEN	COMMENTS
Pinworm disease	Two doses of 1 tablet/50 lb	Repeat 7 days later	This regimen is designed to reduce the risk of reinfection. However, if not practical, repeat the regimen the next day.
Threadworm,* large roundworm,* hookworm,* and whipworm* disease	Two doses of 1 tablet/50 lb	Repeat the next day	Alternatively, a single dose of 2 tablets/50 lb may be given. However, a higher incidence of side effects should be expected.
Creeping eruption	Two doses of 1 tablet/50 lb	Repeat the next day	If active lesions are still present 2 days after completing this regimen, a second course is recommended.
Symptoms of trichinosis* during the invasive phase of the disease	Two doses of 1 tablet/50 lb	Repeat for 2 to 4 successive days	The optimal dosage for the treatment of trichinosis has not been established.

The recommended maximal daily dosage is 3 g (6 tablets).

*Clinical experience with thiabendazole for treatment of each of these conditions in children weighing less than 30 lb has been limited.

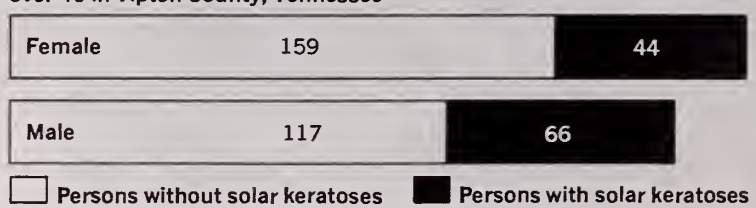
What it means to live and work in Tipton County, Tennessee

Persons who are white and over 40 have one chance in four of having solar keratoses... which may be premalignant

An epidemiologic study* conducted in Tipton County, Tennessee, revealed that 28.5% of white persons over 40 had solar keratoses; most had multiple lesions. Cluster sampling projected an estimated prevalence of 32.5% for white males and 19.5% for white females.

Though this is an unusually high percentage of affected persons, these lesions can occur in any white population, wherever people work or play out of doors.

Prevalence of solar keratoses in white persons over 40 in Tipton County, Tennessee



*Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey.



Solar, actinic, senile keratoses

Called by many names, the typical lesion is flat or slightly elevated, brownish or reddish in color, papular, dry, adherent, rough, sharply defined; usually multiple lesions, chiefly on exposed portions of the skin.

Sequence/selectivity of response

Erythema in areas of lesions may begin after several days of therapy; height of reaction (only in affected areas)* usually occurs within two weeks, declining after discontinuation of therapy. Since this response is so predictable, lesions that do not respond should be biopsied to rule out the presence of a frank neoplasm.

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Cosmetic results are highly favorable. Incidence of scarring is low—important with multiple facial lesions. Efudex should be applied with care near the eyes, nose and mouth.

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Contraindications: Patients with known hypersensitivity to any of its components.
Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.
Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.
Adverse Reactions: Local—pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported—insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.
Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.
How Supplied: Solution, 10-ml drop dispensers—containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.
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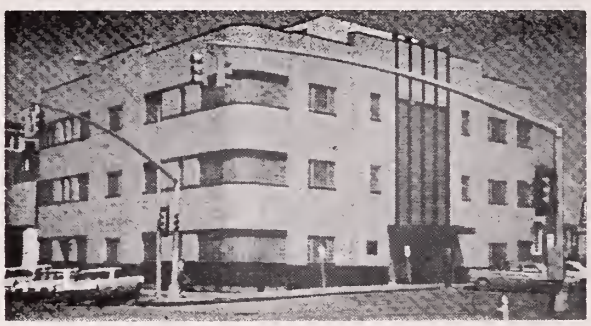
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The JOURNAL
of the Oklahoma State Medical Association

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CONTRIBUTIONS

Articles accepted for publication, including manuscripts of annual meeting papers, are the sole property of *The Journal* and must not have been published elsewhere. Authority for approval of all contributions rests with the Editorial Board, and the Board reserves the right to edit any material submitted. Manuscripts should be typewritten, double spaced and submitted in original and one copy. Receipt of manuscripts will be acknowledged and unused manuscripts returned. Used manuscripts will be returned on request. *The Journal of the Oklahoma State Medical Association* is not responsible for the statements or opinions of any contributor.

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NEWS

Members of the Oklahoma State Medical Association, the constituent societies of the association, and all readers in general are invited to supply news items of general interest to the profession.

ADVERTISING

All advertising copy must be approved by the Editorial Board before acceptance for publication. General and miscellaneous advertising rates will be sent on request.

EDITING SERVICE

The Editorial Board reserves the prerogative to submit contributions to a Medical Editing Service when warranted. If such is felt necessary, the Editor will contact the author for approval, informing him that there will be modest charge for this service.

REPRINTS

Authors will receive reprint order forms from the Transcript Press, P.O. Drawer 1058, Norman, Oklahoma 73069, prior to final publication of their articles. Other requests for reprints must be made to the Transcript Press within 30 days after publication.

BACK ISSUES

Microfilm copies of back issues of *The Journal* may now be purchased from University Microfilms, 300 North Zeeb Road, Ann Arbor, Michigan 48106.

OSMA JOURNAL / *the last word*

Effective May 1st, 1972, only Bureau of Narcotics and Dangerous Drugs Official Order Forms will be valid for transactions involving any controlled substance in either Schedule I or Schedule II. Previously physicians were being allowed to continue using the old IRS Narcotics Order Forms for such transactions. The old forms should be sent to BNDD Registration Branch, P. O. Box 28083, Central Station, Washington, D. C. 20005. New order forms may be acquired by writing to the Registration Branch.

Oklahoma physicians were paid $1,895,300 by the state's Department of Institutions, Social and Rehabilitative Services during the month of February. This amount represented 47,300 individuals receiving services. It also includes about $430,000 to cover deductible and co-insurance payment for individuals over age 65 who are still on welfare.

For nearly a century the American Medical Association has advocated the creation of a separate Department of Health. Now nearly 80 members of the U. S. House and Senate have introduced legislation along this line. One of the chief sponsors for the move is a former Secretary of HEW, Senator Abraham A. Ribicoff (D-Conn.). The legislation, which would break up HEW into three departments, runs counter to President Nixon's plan for government reorganization. His plan calls for merger of HEW into a new, even bigger department of Human Resources. Some sponsors of the bill have indicated they might compromise on two departments—one for Health and Welfare and one for Education. The AMA House of Delegates in 1873 adopted a resolution calling for a separate federal department "as a means of promoting sanitary science and the protection of the public health." This stand has been reaffirmed numerous times, the earliest in 1891 and the latest in 1970.

Discrimination against physicians has been charged by the AMA in a protest to the Federal Price Commission over the administration's Economic Stabilization Program. The protest emphasized that the association supports efforts to curb inflation, but pointed out that physicians are "very much concerned that the economic restrictions imposed upon them do not have equal application to all segments of the economy." It went on to say that professional fees, such as lawyers, outside the health profession were not subject to limitations and that "manufacturers, retailers and sellers of services generally are entitled to full pass-through of their increased costs."

Residents and interns have been formally invited to become regular AMA members. The invitation was extended in an AMA letter to approximately 40,000 residents and interns who became eligible for membership this year. Annual dues will be $20 and the potential new members were told to direct membership inquiries to their county medical society.

Physicians who have not yet posted signs advising patients that a list of base fee schedules is available for examination are urged to do so by the OSMA. Wage-price guidelines issued last December by the Price Commission require that physicians and other providers post such a sign "in a prominent place." Those failing to comply are subject to a fine of $5,000 upon conviction of willful violation. IRS agents have been conducting spot checks throughout the state to determine whether the regulations are being followed. A suggested sign, prepared by the OSMA, was printed in the April issue of the OSMA News. The wording is as follows: "In compliance with the economic stabilization program, base prices for services are available at receptionist's desk." The Oklahoma IRS office has said that a sign with this wording would fulfill the requirements. □

Will his return to work mean the return of undue psychic tension?



When it's mandatory to keep the post-coronary patient calm, consider Valium (diazepam).

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Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect. *Adults*: Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients*: 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children*: 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

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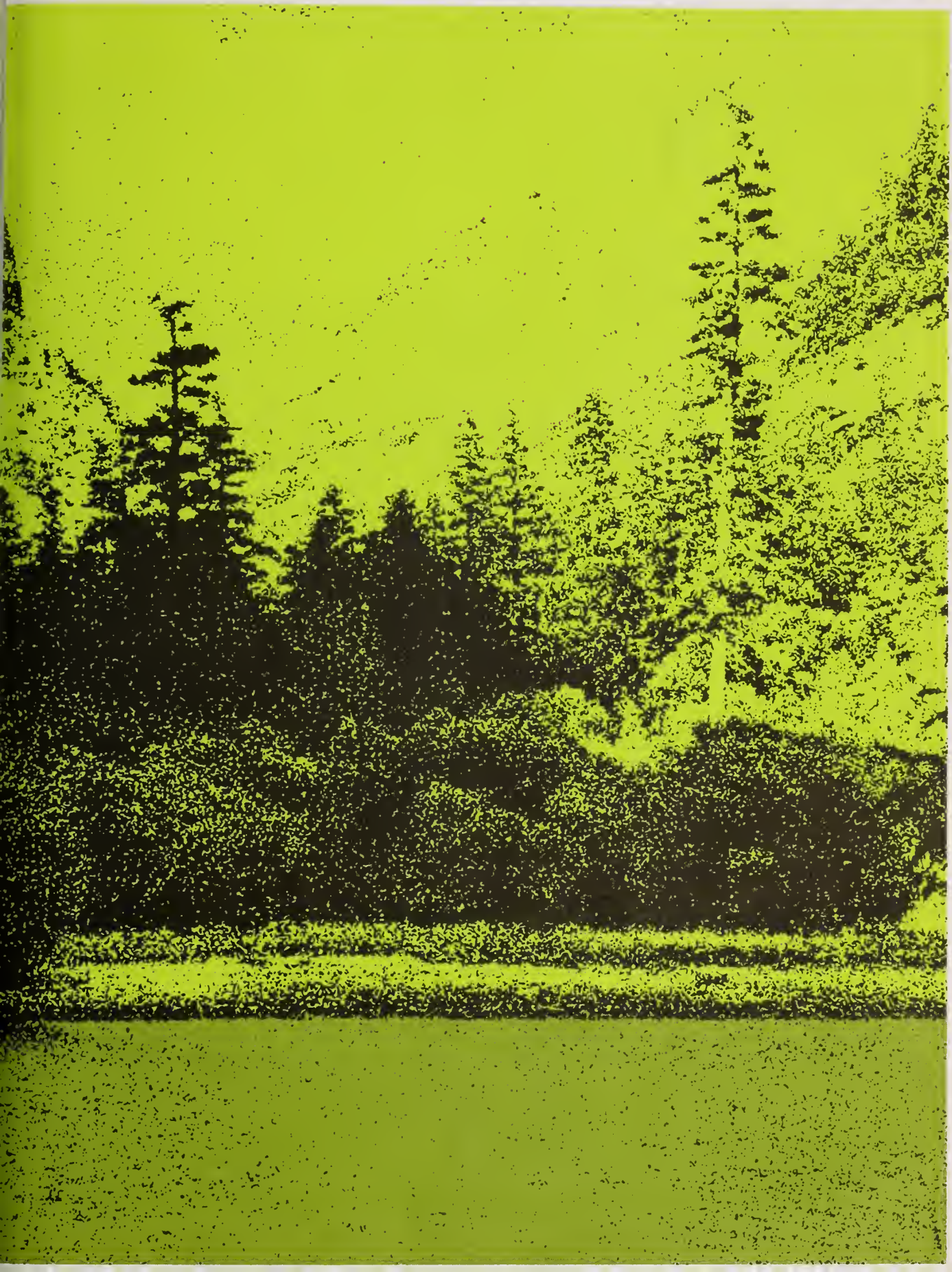
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BALCONY

JOURNAL

Volume 65—Number 6—June 1972

OKLAHOMA STATE MEDICAL ASSOCIATION





Everybody experiences psychic tension.



Most people can handle this tension.



Some people develop excessive psychic tension and need your counseling,



and a few may need counseling
and the psychotropic action of Valium® (diazepam).

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While Valium can be a most helpful adjunct to your counseling, it should be prescribed only as long as excessive psychic tension persists and should be discontinued when you decide it has accomplished its therapeutic task. In general, when dosage guidelines are followed, Valium is well tolerated (see Dosage). For convenience it is available in 2-mg, 5-mg and 10-mg tablets.

Drowsiness, fatigue and ataxia have been the most commonly reported side effects.

Until response is determined, patients receiving Valium should be cautioned against engaging in hazardous occupations requiring complete mental alertness, such as driving or operating machinery.

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JUNE
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What's on your patient's face...

may be more important than his chief complaint

The lesions on his face may be solar/actinic — so-called "senile" keratoses...and they may be premalignant.

Solar, actinic or senile keratoses

These lesions may be called by several names, but they usually can be identified by the following characteristics: the typical lesion is flat or slightly elevated, of a brownish or reddish color, papular, dry, rough, adherent, and sharply defined. They commonly occur as multiple lesions, chiefly on the exposed portions of the skin.



Patient P.T. seen on 3/29/67 shows typical lesions of moderately severe keratoses. Note residual scarring on ridge of nose from previous cryosurgical and electrosurgical procedures.*

Sequence of therapy/ selectivity of response

After several days of therapy with Efudex® (fluorouracil), erythema may begin to appear in the area of the lesions; the reaction usually reaches its height of unsightliness and discomfort within two weeks, declining after discontinuation of therapy. This reaction occurs in affected areas. Since the response is so predictable, lesions that do not respond should be biopsied.

Acceptable results

Treatment with Efudex provides highly favorable cosmetic results. Incidence of scarring is low. This is particularly important with multiple facial lesions. Efudex should be applied with care near the eyes, nose and mouth.



Patient P.T. seen on 6/12/67, seven weeks after discontinuation of 5%-FU cream. Reaction has subsided. Residual scarring not seen except for that due to prior surgery. Inflammation has cleared and face is clear of keratotic lesions.*

*Data on file, Hoffmann-La Roche Inc., Nutley, N.J.

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Indications: Multiple actinic or solar keratoses.

Contraindications: Patients with known hypersensitivity to any of its components.

Warnings: If occlusive dressing used, may increase inflammatory reactions in adjacent normal skin. Avoid prolonged exposure to ultraviolet rays. Safe use in pregnancy not established.

Precautions: If applied with fingers, wash hands immediately. Apply with care near eyes, nose and mouth. Lesions failing to respond or recurring should be biopsied.

Adverse Reactions: Local — pain, pruritus, hyperpigmentation and burning at application site most frequent; also dermatitis, scarring, soreness and tenderness. Also reported — insomnia, stomatitis, suppuration, scaling, swelling, irritability, medicinal taste, photosensitivity, lacrimation, leukocytosis, thrombocytopenia, toxic granulation and eosinophilia.

Dosage and Administration: Apply sufficient quantity to cover lesion twice daily with nonmetal applicator or suitable glove. Usual duration of therapy is 2 to 4 weeks.

How Supplied: Solution, 10-ml drop dispensers — containing 2% or 5% fluorouracil on a weight/weight basis, compounded with propylene glycol, tris(hydroxymethyl)aminomethane, hydroxypropyl cellulose, parabens (methyl and propyl) and disodium edetate.

Cream, 25-Gm tubes — containing 5% fluorouracil in a vanishing cream base consisting of white petrolatum, stearyl alcohol, propylene glycol, polysorbate 60 and parabens (methyl and propyl).

This patient's lesions were resolved with

Efudex® (fluorouracil)

5% cream/solution ....a Roche exclusive

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Thank You, Doctor



Your continuing cooperation with the American Association of Medical Assistants has been generous. With your support our organization has achieved a membership of 14,000 medical assistants in more than 400 chapters in 45 states, District of Columbia and Puerto Rico.

Since our first organizational meeting 15 years ago, we have worked toward the primary goal of providing educational opportunities to the medical assistant in the doctor's office. In a short decade and a half the association has:

- Established and conducted a certification program as an incentive to self-education.
- Developed curricula for medical assisting programs in hundreds of junior and community colleges.
- Carried on a continuing education program for medical assistants through seminars, workshops and a professional bi-monthly journal.
- Published career materials and established a scholarship loan fund to help recruit future medical assistants.
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– George Sarton, from "The History of Medicine Versus the History of Art"

Would it be useful in clinical practice to have government predetermine drugs of choice?

Opinion

Results of a survey of physicians:

13.3%
Yes, it would be useful.

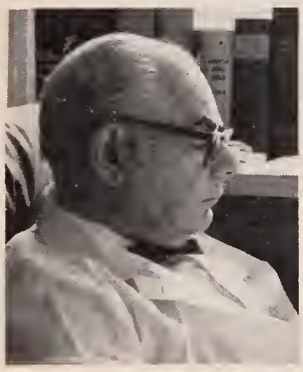
86.7%
No, it would not be useful.

Dialogue

Would it be useful in clinical practice to have government predetermine drugs of choice?

Doctor of Medicine

Walter Modell, M.D.,
Professor of Pharmacology,
Cornell University
Medical College,
Editor,
Clinical Pharmacology
& Therapeutics,
Drugs of Choice,
Rational Drug Therapy



The proposition that government should determine one or two "drugs of choice" within a given therapeutic class reflects the belief that a similarity in molecular structure insures a close similarity in pharmacologic effect. But this is by no means the rule. An obvious example would be in the field of diuretics, where a small change in chemical structure accounts for substantial differences in concomitant effects such as potassium excretion.

Any attempt to dictate the "drug of choice" would be complicated by the fact that some populations demonstrate a bimodal distribution in their reaction to drugs. If the data on drug response are mixed for the total population, one drug will appear to be as useful as the other. But if drug response is reported separately for different segments of the population, drug A will be found to be better for one group and drug B for the other.

It may, of course, be possible to determine drugs of choice in particular categories on a broad statistical basis. But there are always certain patients in whom a drug produces odd, unpredictable or idiosyncratic reactions. So, though a drug might statistically be the most useful one in a given situation, individual variations in response might make it the *incorrect* one.

The point I wish to make is that if two, three, four or more drugs in one class are of approximately equal merit, that in itself is justification for their availability. Exceptional cases do arise in which one drug would be useful to a certain segment of the population and another drug would be of no use at all. In the practice of medicine, the physician must be prepared to treat the routine as well as the unusual case.

Another objection to the determination of a drug of choice is that precise statements of *relative* efficacy are very difficult to make—much more difficult than statements of efficacy. For example, in testing drug efficacy, it is easy to determine the difference between a drug that is effective in treating a condition and one that is not at all effective. Thus, it is fairly easy to determine whether a drug is more effective than a placebo. But if you compare one drug that is effective with another drug that is also effective, and the relative differences between them are very slight, statements of relative efficacy may be very difficult to make with assurance.

I do not mean to imply that relative efficacy statements are not useful or can never be made. With some groups of drugs (e.g., analgesics), extensive study and precise methodology have yielded useful information on relative efficacy. But in most situations, such information can be acquired only through studies encompassing three to five years of use in many more patients than are used to compare drugs with a placebo for the introduction of a drug into commerce. It is really only after practitioners use a drug extensively that relative safety and efficacy in practice can really be determined.

The Bureau of Drugs has suggested the package insert as a possible means of communicating information on relative efficacy of drugs to the physician. I find this objectionable, since I do not believe the physician should have to rely on this source for final scientific truth. There is also a practical objection: Since few physicians actually dispense drugs, they seldom see the package insert. In any event, I would maintain that the physician should know what drug he wants and why without depending on the government or the manufacturer to tell him.

Undoubtedly, physicians are swamped by excessive numbers of drugs in some therapeutic categories. And I am well aware that many drugs within such categories could be eliminated without any loss, or perhaps even some profit, to the practice of medicine. But, in my opinion, neither the FDA nor any other single group has the expertise and the wisdom necessary to determine the one "drug of choice" in all areas of medical practice.

Maker of Medicine

Kenneth G. Kohlstaedt, M.D.,
Vice President,
Medical Research,
Eli Lilly and Company



In my opinion, it is not the function of any government or private regulatory agency to designate a "drug of choice." This determination should be made by the physician after he has received full information on the properties of a drug, and then it will be based on his experience with this drug and his knowledge of the individual patient who is seeking treatment.

If an evaluation of comparative efficacy were to be made, particularly by government, at the time a new drug is being approved for marketing, it would be a great disservice to medicine and thus to the patient—the consumer. For example, when a new therapeutic agent is introduced, on the basis of limited knowledge, it may be considered to be more potent, more effective, or safer than products already on the market. Conceivably, at this time the new drug could be labeled "the drug of choice." But as additional clinical experience is accumulated, new evidence may become available. Later, it may be apparent that the established products should not be so easily dismissed.

Variation in patient response to drugs constitutes one of the major obstacles to the determination of "drugs of choice." We are just beginning to open the door on pharmacogenetics, but it is evident that genetic differences cause wide variations in the way drugs are absorbed, metabolized, etc. This fact alone is sufficient to make unrealistic the idea that there is one drug in each class to be used for every human being.

The problem of determining relative drug efficacy is an extremely complicated one. Comparison with other drugs of the same class should not be a prerequisite for marketing a new substance. In some therapeutic areas, it may be difficult to make accurate comparisons. For example, in the treatment of infections it is not possible to conduct crossover studies. Recovery may be influenced by factors which cannot be controlled or measured, i.e., natural host resistance and virulence of infective agents. A drug's acceptability must often be judged on the basis of its own performance, and this may be limited to experience in a relatively small patient population. If the introduction of a new drug must await the adequate establishment of relative efficacy, the duration of clinical trial and extent of studies would be greatly prolonged, particularly for rare or unusual conditions. The availability of a new drug would be delayed. Many patients might suffer needlessly and lives might be lost.

Relative efficacy can best be established by experience in a general patient population through regular channels of clinical practice. The physician considers the patient as a whole, which means the patient often has multiple problems and drugs must be selected with this in mind. Hence, a "drug of choice" in an uncomplicated case may not be the best drug for a patient with associated problems. Publication of well-controlled studies in medical journals may provide comparative evidence; discussions at medical meetings, presentations at postgraduate courses, and the new audiovisual technology may bring evidence to physicians on comparative therapy. In a free medical marketplace, a drug that does not measure up will fall into disuse. For example, broad clinical experience has established vitamin B_{12} as the "drug of choice" for the treatment of primary pernicious anemia. No amount of advertising or promotional effort by the manufacturer could increase the use of liver extract for this anemia. However, a physician may wish to employ parenteral liver preparations for a special purpose.

In the field of surgery, peer review in the hospital has brought significant improvement in the use of new techniques and procedures. Something of this nature would be useful in the area of drug therapy. However, it should be developed by the medical profession itself and would necessitate, for its proper function, an improvement in the dissemination of reliable data on clinical pharmacology of drugs under consideration.

Ideally, information on the relative efficacy of drugs should be gathered and assessed by the physicians who actually administer the specific agents to a specific patient population. To do this, they will need even more information on the drugs they use—information that the pharmaceutical manufacturers must begin to provide if government regulation of "*drugs of choice*" is to be avoided.

Opinion & Dialogue

What is your opinion, doctor?
Send us your comments on the above issue.

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Health Education in Oklahoma

PHYSICIANS AS well as the public are becoming accustomed to the term "health crisis." American medicine is in a state of ferment. New legislation, the reports of public and private commissions, the torrent of articles and books concerned with health and medical care, and the many experimental programs, both in medical education and in the organization and delivery of health services are testimony to this fact. Fundamental to the discussions concerning health services is the issue of the supply of health manpower. Ultimately the responsibilities for the supply of health manpower fall on the shoulders of the medical and other health professional schools and their clinical laboratories (teaching hospitals).

In medical journals which serve as the organs of local, national or regional medical organization, the discussion usually centers on the role of the practicing physician. This is appropriate, but no individual or group of practicing physicians alone can bring about major changes in the supply of physician manpower. The responsibility for this again falls on the schools of medicine. Despite the often used cliche of "town versus gown," all physicians, whether they be in the private practice of medicine or full time faculty members of a school of medicine or other health related schools, are involved in this incredibly large and complex problem. All persons connected with the health professions will have to contend with the problem for the next several years, and I would like to present some of the reasons for this.

In any city in which a school of medicine is located, it is not uncommon at any gathering of physicians to hear the statement that doctors are divided into two categories —the practicing physicians and the university physicians. This division is artificial and incorrect as it relates to certain fundamental responsibilities. Physicians, certainly those in the clinical departments of the University of Oklahoma Health Sciences Center, are also practicing physicians—they practice at the Health Sciences Center and its affiliated hospitals. But both groups are inexorably involved in the task of producing health manpower.

In October of 1970, the Carnegie Commission on Higher Education published a special report with recommendations entitled, "Higher Education and the Nation's Health Policies for Medical and Dental Education." This report is having a significant impact on health legislation, education and planning. Among the major goals of the recommendations of the Carnegie report is the production of more health care personnel, a better distribution of such personnel, and the establishment of new types of health educational systems. During the decade of the 70's the report states that the number of places for training physicians should be expanded by 50% and for dentists by 20%. Furthermore, the training opportunities for all health personnel should be expanded substantially. In order to provide for this expanded student census, existing schools are urged to increase their enrollment.

The recently enacted legislation entitled, "The Comprehensive Health Manpower Training Act of 1971," has very important implications for all persons in the health professions, but particularly physicians. Some of the important provisions of this legislation which are important to medical schools and hence to the medical profession are:

1. Schools will continue to be eligible for grants to be awarded in direct support of education. However, priority will be given to those schools which continue to increase the number of students admitted.

2. Substantial bonuses will be offered to medical schools which effect curricular changes resulting in graduation in 36 months or less.

3. Special project grants will be made to schools to encourage more effective approaches to the organization and delivery of health services through the team approach and the use of computer technology.

4. Special grants will be made to schools which develop programs designed to encourage the enrollment of those students who are likely to practice in shortage areas.

5. There will be new and significant forgiveness provisions in student loans for graduates who elect to practice in areas

Continued on page xvi



Now that the annual meeting of OSMA is over, it gives the staff and officers an opportunity to evaluate and to carry out the directives of the Board of Trustees and House of Delegates.

Several significant actions were taken:

1. OSMA support for the Health Sciences Center in its present crisis was assured by an action of the House of Delegates, which deserves the attention of all physicians in the State.

2. The decision to poll the membership to obtain your opinion on new abortion legislation points up the reluctance of the House of Delegates to formulate a position on this explosive issue without being certain of the feelings of the total membership. Readily available abortion, as the law allows in some states, goes against the very basic tenets of physicians' life-long ideals. On the other hand, pressure from the public and legislature may force some legislation, in which case, OSMA should have some maximum input into any laws that are passed.

3. The passage of Resolution #14 encouraging physicians to notify their patients that all relationships between physicians and third parties will cease (except Medicaid), and that in the patient's best interest no third party will be allowed to come between a patient and his doctor. This very basic resolution is capable of freeing us all from the endless entanglements of dealing with third parties. It could represent a turning point in improved doctor-patient relationships, since currently the most common cause of grievances is a misunderstanding between a third party and the patient, which is then blamed on the doctor. By the simple mechanism of not taking assignment, we can eliminate all of the bickering with third parties, reduce to nil the most common cause of complaint, and in the long run insure our freedom. Also, of course, this would make our patients our employers and not the government or an insurance company. Surely this is a desirable goal.

Other actions of the annual meeting are described in this and subsequent issues of *The Journal* and are recommended reading. □

Sincerely,

S. R. McCampbell, MD

OSMA JOURNAL/scientific

Malignant Melanoma of the Eye, Metastatic After Twenty-nine Years: A Case Report

FRANK G. GATCHELL, MD
DAN MINOR, MD

A patient with malignant melanoma of the left eye removed twenty-nine years previously presented as pancreatitis with pseudocyst formation and metastases to the pancreas and transverse mesocolon.

I INTRODUCTION

MALIGNANT MELANOMA has been an enigma to physicians for many years due to its unpredictability. The potential to metastasize with low survival rates at five and ten years has been common knowledge. Before 1940 and the use of radical surgery for malignant melanoma the five and ten year survival rates were approximately twelve percent.[1] Booher[2] in his review, *Recognition and Treatment of Melanoma*, has noted that now with localized melanoma the ten year survival rate is approximately sixty-two percent. However, as may be noted by this case report, ten year followups may not suffice in some cases. McDonald,[6] in 1948, gave the approximate rate of incidence of malignant melanoma as 1.6 per 100,000 males and 2.0 per 100,000 females per year. Approximately 1.8 melanomas are found among every 1.5 million nevi. Davis, Herron and McLeod[3] studied the incidence of malignant melanoma in Australia between the years 1963 and 1965 and reported an incidence of 16.4 per 100,000 as compared to the 2.0 in England and 2.6 in the United States.

The above incidence figures are overall figures of all malignant melanomas and do not represent the incidence of malignant melanoma of the eye which is the lesion in the case for discussion. Pack[8] in his analysis of the location of melanomas, gives the following percentage rates for location: Twenty-seven percent occurred on the lower extremity, 9.8 percent on the upper extremity, 2.9 percent subungually, 24 percent on the trunk, 22 percent on the head and neck, 10 percent at other less usual sites and 2.4 percent presented with an unknown primary site.

Regardless of the site of the original melanoma, the followup studies have shown a rather erratic pattern of survival. Hendrix,[5] in a review article studying 216 cases at the University of Michigan, presented thirty-five of the 216 as unusual survival patterns in metastatic melanoma. Of these cases, approximately one-half presented with distant metastases at the time of original diagnosis. Thirty-five of the 216 cases lived

From the Department of Surgery, Oklahoma City Clinic, 301 Northwest Twelfth Street, Oklahoma City, Oklahoma 73103.

longer than five years with a 16.2 percent survival at five years. The whole group of 216 had an average age of 44.7 years with 58 percent of these patients being men. The average age of those surviving beyond five years was 42.5 with 55 percent of them being male. Three of the thirty-five had a bizarre morphologic cell type, the others being more typical of malignant melanoma. The age and sex ratio tend to indicate that there is no real difference between the survivors and those that succumbed to the disease. Reed and Kent[9] reported a sixty-six year old male with a solitary lung metastasis from an intraocular melanoma removed thirty-one years previously. The following case report is that of a patient presenting with metastases after surviving twenty-nine years, which is longer than any of the cases reported by Hendrix.[5]

II CASE REPORT

The patient is a seventy-two year old white female (J. A.) who, at age forty-three, underwent an enucleation of the left eye for acute glaucoma. Microscopic report of the left eye revealed acute glaucoma secondary to malignant melanoma.

The patient was then lost to followup until age seventy at which time she presented with cholelithiasis. She underwent cholecystectomy elsewhere and at the time of surgery a tumor was found in the pancreas which was felt to be pancreatic carcinoma, although it was not biopsied at the time. She had several attacks of epigastric pain and vomiting following surgery, and several months before her next hospitalization she complained of upper abdominal pain and vomiting. Two years following cholecystectomy the patient was hospitalized with upper abdominal pain and vomiting. Laboratory results revealed serum amylase of 305; electrolytes, fasting blood sugar, BUN and CBC were all within normal limits. Urinalysis revealed two plus ketones. The patient was treated with nasogastric suction and Pro-Banthine® with the initial diagnosis of acute pancreatitis. A liver scan was within normal limits. Chest x-ray was normal. X-ray films of the abdomen showed no pancreatic calcification and an intravenous cholangiogram provided no significant information. Upper gastrointestinal series revealed pressure changes on the greater curvature of the antrum of the stomach and on medial margins of the second and third portions of the duodenum in the area of the head and body of the pancreas. At exploratory laparotomy a large pseudocyst was found in the head of the pancreas. Several dark areas on the body of the pancreas and one in the transverse mesocolon were also found. Needle biopsies of these revealed metastatic malignant melanoma with the following notation: "A spindle type cell laden with dark brown pigment strongly suggestive of metastatic melanoma from the eye."

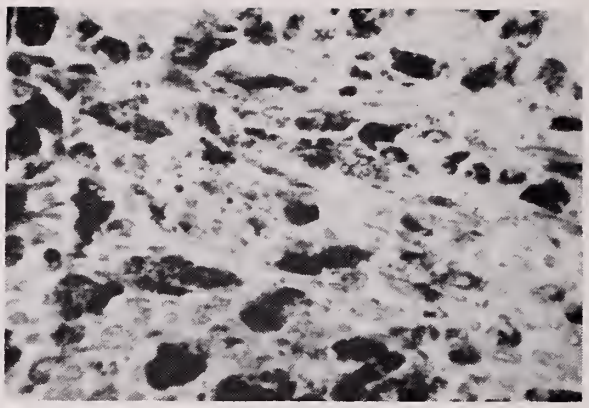


Figure I. Microscopic section of melanoma of eye (hematoxylin and eosin stain x 150).

Figures I and II. The original slide of the melanoma of the eye was obtained and compared with slides of the metastatic tumor. The pathologist reported the two in-

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Frank G. Gatchell, MD, graduated from the University of Oklahoma School of Medicine where he is now Clinical Assistant Professor of Surgery. Certified by the American Board of Surgery, Doctor Gatchell is a Fellow of the American College of Surgeons, a member of the Oklahoma Surgical Association, the Society of Head and Neck Surgeons, Southwestern Surgical Congress and President of the Oklahoma Chapter of the American College of Surgeons.

Dan Minor, MD, graduated from the University of Oklahoma School of Medicine in 1971 and is currently serving a rotating internship at the University of Oklahoma Health Sciences Center.

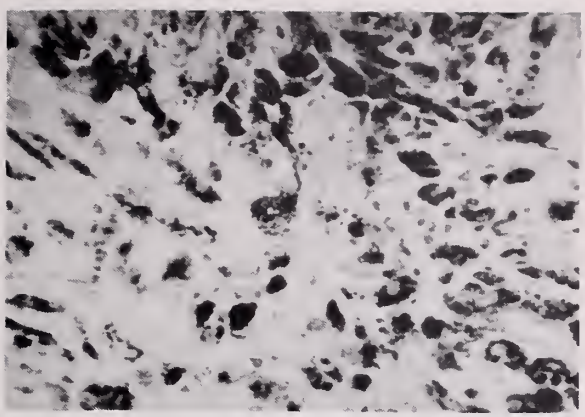


Figure II. Microscopic section of metastatic melanoma to transverse mesocolon. Note striking similarity to Figure I (hematoxylin and eosin stain x 150).

distinguishable (see Figures I and II). It is interesting to note that the diagnosis of malignant melanoma was unknown to the patient although she did know about the acute glaucoma. The pathologist made the diagnosis of metastatic malignant melanoma from the eye without any information concerning the patient's loss of the left eye.

CREDITS

The aid of Raymond F. Hain, MD, pathologist, is acknowledged. □

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A cocktail party is scheduled for Friday evening and a buffet dinner Saturday night.

The meeting has been planned by the joint Medical-Legal Relations Committee of the OSMA and OBA. Registration fee for the two-day meeting is $40 to cover the cost of course materials, the cocktail party Friday and one ticket to the dinner Saturday evening.

Advanced registration should be directed to the Oklahoma State Medical Association, Attention Ed Kelsay, 601 N. W. Expressway, Oklahoma City, Oklahoma 73118. □

The Management of a Patient With A History of Penicillin Hypersensitivity

L. JOHN DAVIS, MD

True penicillin hypersensitivity is relatively rare, however, a history of possible penicillin hypersensitivity is not infrequently obtained. A rational approach toward managing such a patient is discussed.

DESPITE THE RISK of allergic reactions, the penicillins are often the drugs of first choice for many infections because of their bactericidal activity and low toxicity. However, the clinician is frequently thwarted in this choice by a sometimes dubious history of penicillin allergy. For the clinician to reach an intelligent decision with such a history, at least three pieces of information must be evaluated. He must know and consider the range of manifestations which occur with penicillin hypersensitivity and have a knowledge of the prognostic implications associated with a particular reaction pattern. He must know which laboratory methods for the detection of penicillin hypersensitivity are easy, practical, and yet safe and dependable. The clinician must make a meaningful evaluation of the alternative risks involved in a given patient both with and without penicillin therapy. Because of the short period of time that penicillins have been used therapeutically, research on penicillin hypersensitivity is still incomplete and, therefore, the answers to many of the above questions are contested and partial at best. An attempt will be made in this discussion to review some current opinions on this subject.

From the Department of Pediatrics and the Children's Memorial Hospital, University of Oklahoma Health Sciences Center.

At the time of preparation of this paper, Doctor Davis was a fourth year medical student at the University of Oklahoma School of Medicine.

Worldwide, the incidence of allergic reactions to penicillin is reported to vary from 0.7% to 10%.[1] However, it is generally felt that the incidence of true penicillin . . . hypersensitivity is approximately 5% in adults and considerably lower in children.[2] However the incidence of positive history for penicillin allergy is considerably above any of these figures.

The following is a brief description of the various known patterns of reaction to penicillin, . . . which should be used as an aid in evaluating histories. Penicillin reactions may be considered in three general categories, *immediate*, *accelerated*, and *delayed* reactions. Reactions which are considered immediate usually occur within 20 minutes. This type reaction may either consist of flushing, generalized pruritus, and urticaria or it may be of the anaphylactic type with laryngeal edema, bronchial spasm, hypotension, and shock.[2] For the immediate type reaction to occur, antibodies must be present in the patient as the result of previous exposure to penicillin[3] which may have occurred up to a decade or more earlier.[4]

Accelerated reactions to penicillin have their onset within 30 minutes to about 48 hours (occasionally within a few minutes) after initiation of therapy. They resemble the immediate type reaction, but are usually less severe and rarely, if ever, include hypotension or laryngeal edema. Erythema, with or without fever, is common.

Most penicillin reactions are the delayed type, with the onset several days or weeks after the penicillin was administered. The term "late" or "delayed reactions" refers to the time elapsing between administration of penicillin and the occurrence of the clinical symptoms and does not imply that such symptoms are due to a delayed (tuberculin type) hypersensitivity, i.e. an immunological mechanism involving sensitized lymphocytes instead of circulating antibodies.[7] Most of these delayed reactions are urticarial or

erythematous, and may or may not be accompanied by fever.[2] Occasionally only fever occurs. A serum-sickness-like syndrome consisting of urticaria, joint swelling and pain, fever and proteinuria sometimes occur. The urticaria can persist for months or years and may be prolonged by traces of penicillin in milk or other foods. Rarely, large doses of penicillin induce an immune hymolytic anemia; a few cases of thrombocytopenia, granulocytopenia, neuritis, carditis and acute renal failure have been reported.[8, 12]

The most common cause for the misdiagnosis of "penicillin allergy" in children is the viral exanthema. Many children who are treated with penicillin for malaise and upper respiratory symptoms in the prodromal phase of a viral exanthema are subsequently falsely labeled as having had an untoward penicillin reaction. The diagnosis of penicillin allergy should not be doubted when the symptoms consisted of angioneurotic edema or severe constitutional serum-sickness-like reactions. The diagnosis may be qustioned, retrospectively, when the child developed a nonspecific generalized erythematous maculopapular rash (on the third and fourth day following administration of penicillin) which could have been due to a viral exanthema.

In recent years there have been many attempts to develop a method for detecting penicillin antibodies. Such a procedure, if dependable, would be of immeasurable aid to the clinician presented with a patient with such a history. Although structural characteristics of many drugs indicate that they cannot irreversibly combine with proteins, allergies may develop to their intermediate metabolic or degradation products which form the required immunogenic hapten-protein-conjugates and induce antibody responses. In penicillin allergy, the haptenic system and the nature of drug sensitivity are now being determined.

Investigations have shown that penicillin gives rise to a major antigenic determinant —the penicilloyl group—which may be conjugated to a protein residue which increases the possibility of sensitization.[5, 6]

Since proteins are potent immunogens, there is a substantial risk of sensitizing normal individuals if a penicilloyl is used for skin testing. In recent years, a skin test substance has been developed consisting of the major determinants of penicillin with a polymerized lysine carrier called penicilloyl-polysine (PPL); this appears to be less antigenic. The test is reproducible and the antigen in test doses has been reported as nonsensitizing in man.[7] Another skin test material now being investigated is "*minor-determinant-mixture*" (MDM) which contains a solution of penicillin and several of its degradation *products*.[2] Since PPL and MDM are not generally available, a scratch test may be used with various dilutions of penicillin, followed by an intradermal test using progressively increasing concentrations of penicillin. Although severe systemic reactions have been reported following initial intradermal test with penicillin,[8] this complication could probably be lessened by using a scratch test prior to the intradermal test. However, recently, the anaphylactic death of a patient following administration of a scratch test with crystalline penicillin in a solution of 40,000 international units (IU) per ml has been reported.[9] Currently, the scratch test is recommended first, starting with 1000 IU per ml followed by 10,000 IU per ml which is administered intradermally. These skin tests with penicillins appear to be more dangerous than tests using PPL.

Skin-sensitizing antibodies specific for major penicilloyl antigenic (PPL) determinant are usually associated with immediate and early urticarial reactions (minor reactions). Skin-sensitizing antibodies specific for minor penicillin antigenic determinants are associated with sudden life-threatening anaphylactic reactions and thus can be detected more readily by skin testing with old solutions of penicillin.[10] It has been determined that the major determinants are also involved in a few anaphylactic reactions.[11]

Administration of penicillin can also cause the formation of hemagglutinating antibodies which may be detected by serologic

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Lloyd John Davis, MD, was graduated from the University of Oklahoma College of Medicine in 1969, where he is now taking a residency in radiology. Doctor Davis is a member of the Alpha Omega Alpha.

tests. Their clinical significance is uncertain at this time. Some individuals with PPL-positive skin tests do not develop allergic reactions although they have high titers of hemagglutinating antibodies in much the same manner as bee keepers have blocking antibiotics against bee venom.[12] Whatever their nature, they do not seem to be involved directly in untoward reactions following the administration of penicillin. Recently a modification of the passive hemagglutination technique showed that 97% of a group with no history of penicillin allergy had these antibodies.[13]

In a recent study of 172 children, half of whom had a history of penicillin sensitivity, skin testing and hemagglutination determinations were performed to determine the incidence of substantiated penicillin hypersensitivity.[14] The sensitivive subjects were tested no less than one month and no more than one year following the untoward reaction. Of 73 sensitive subjects, a diagnosis of urticaria could be made definitely in only seven; the remainder gave a history of non-specific erythematous rashes following the administration of penicillin. Only eight percent of those children labelled as penicillin sensitive had positive skin tests to benzyl-penicillin or hemagglutination titers. When skin tests with PPL were also done, the incidence increased to 15%. These findings confirm the suspicion that penicillin hypersensitivity is over-diagnosed in children. Many untoward reactions observed following penicillin administration are not due to penicillin sensitivity. They may be due to the vehicle (e.g., procaine), to the underlying disease process for which the penicillin was prescribed, or to unexplained phenomena.

Rosh and Shinefield[15] also found that some individuals reacted to the PPL alone and to PPL plus its inhibiter, penicilloyl epsilon-amino-caproate. Only those individuals who responded to PPL alone (and not to the mixture with the inhibiter) were considered positive. Such a procedure ideally should be incorporated into all skin testing for penicillin hypersensitivity. They also emphasized the critical time factor in skin testing. The time interval from a previous penicillin injection to the one which results in anaphylactic shock almost always ranges from one to twelve months.[11] Demonstration of penicillin antibodies is most reliable if the interval from the untoward reaction to the time of testing is between one and twelve months.[15, 16] In patients who have had well-documented allergic reactions two to two and one-half months prior to testing, the PPL skin test is positive in 90%, while in patients who have had allergic reaction five to ten years previously, only 25% to 35% respond.[17] In the study of 172 children,[15] no skin or circulating antibodies could be detected in any individual whose untoward reaction had occurred more than 24 months prior to testing.

The dangers of a serious reaction in penicillin therapy or to skin testing is real, but is not absolute. The most serious is the anaphylactic reaction, for while others may be disquieting, they are not life-threatening. Sensitized individuals tend to respond to the second administration of penicillin with a reaction similar to but more violent than their first one.

Skin testing most properly should be limited to patients with an ambiguous history of penicillin reaction; in persons with clear-cut allergic reactions to penicillin it would be of limited value. However, in any case, by choosing an appropriate test schedule beginning with a preliminary scratch test and *then using progressive PPL concentrations,* it is possible to avoid, almost entirely, *systemic reactions* from overdosage in highly sensitive patients. In an analysis of 151 fatalities from anaphylactic penicillin reactions,[11] more than half occurred in the 25-64 year age group; the others were evenly distributed below 25 and over 65 years of age. Ten of the fatalities were below 5 years of age; six of these were two years old or less and two were three months old. Sixty-five percent of the fatalities were in people with atopic histories and most had bronchial asthma. Almost 100% of the fatalities were subjects known to be previous reactors of the immediate type.[11] If the patient with a past history of penicillin allergy proves to have positive skin tests, the risk of reactions with additional penicillin therapy is greatly increased. Of the children studied by Rosh and Shinefield,[15] ten were either challenged

or treated with some form of penicillin. One with a positive history and a positive skin test developed generalized urticaria within 24 hours of the administration of penicillin. The other nine, who had positive histories but no positive skin tests, failed to develop untoward reactions with therapy.[15] Patients with positive PPL skin tests treated with penicillin may fail to develop anaphylactic reactions, although the frequency of severe generalized reactions in PPL positive patients under treatment with penicillin was so high (42%+) that this type of experiment had to be discontinued.[11]

Negative skin tests to penicillin major and minor determinants indicates that there is a very small chance of an acute immediate reaction to penicillin; delayed reactions such as serum sickness cannot be ruled out. Some false positive reactions to major and minor penicillin determinants do occur.

Any allergy testing done by intradermal or scratch technique should be done on an extremity so that a tourniquet can be applied proximal to the test site. Epinephrine 1:1000 injectable should always be at hand in the event of an acute allergic reaction.

In summary, the following procedures are recommended for managing a patient with a history of possible penicillin allergy, if penicillin therapy is indicated. The original untoward reaction should be well-documented and observed if possible. If there is a possibility that the reaction is not due to penicillin (most usually in the delayed type reaction), then the patient should be tested for skin sensitizing and circulating antibodies not less than one month nor more than one year following the untoward reaction.

The absence of demonstrable penicillin antibodies is not an indication for the indiscriminate use of penicillin. If the patient with no penicillin antibodies should develop a serious illness or an illness which does not respond to other antibiotics, then a penicillin should be considered, with preparations made for treating any serious reactions should they occur.

Patients who had penicillin reactions many years previously, may no longer be sensitive; however, penicillin should be used in such patients only if no satisfactory alternative drug is available and preliminary scratch and intradermal tests are negative. Since the tests are not conclusive, parenteral corticosteroids or antihistamines may be administered prophylactically and concomitantly to minimize any allergic response. For the severe and acute allergic reaction, epinephrine is the drug of choice.

If penicillin is urgently needed by a patient with a history of a previous immediate reaction, or if the skin tests are positive and the patient cannot tolerate any alternative drug, rapid desensitization may be carried out. Such circumstances are rare. It must be remembered that this "desensitization" is transient and dependent upon constant antibody depletion. It should be carried out only when equipment for respiratory and circulatory assistance is at the bedside.

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OSMA JOURNAL/special

Benjamin Rush: Physician in Politics

PAUL F. LAMBERT

From 1776 to 1813, Benjamin Rush zealously sought the establishment of a republican utopia. Although he failed, he had a remarkable impact upon American History.

FROM THE COLONIAL period of American history to the contemporary era, physicians have played prominent parts in the affairs of their nation, state, and locality. This was particularly true during that epic age of the republic's birth—from the War for Independence to the War of 1812. The most eminent American physician of this time was Benjamin Rush of Philadelphia. Mourning the doctor's death in 1813, Thomas Jefferson wrote John Adams: "Another of our friends of 76 is gone . . . a better man . . . could not have left us, more benevolent, more learned, of finer genius, or more honest." Adams replied that he also lamented their friend's passing, for he knew "of no character living or dead, who has done more real good in America."

Rush was equally well-known to other luminaries of his generation, for after 1800 he was Philadelphia's leading citizen, and he was famous in both the United States and Europe. In addition to teaching and practicing medicine, his interests encompassed educational reform, scientific pursuits, social reform, psychiatry, and politics. Indeed, Rush was prominent in the movement for Independence from Great Britain, and he was active in the politics of both Pennsylvania and the United States from 1776 to 1790. Moreover, Rush's significance transcends his acquaintances and his accomplishments, for he envisioned the creation of a republican utopia in the New World. Until his death he zealously sought to make his Revolutionary dream become reality.

The development of Rush's desire to create an ideal republic began with his early religious and educational experiences. His pious, Presbyterian mother instilled in the young Benjamin a puritanical devotion to moral and religious values. Two other devout Presbyterians, Samuel Findley and Samuel Davies, also significantly influenced Rush. Thus when he journeyed to Edinburgh, Scotland to study medicine in 1766, his friends there were "chiefly those who are governed by the principles of virtue and religion."

Rush's sojourn at Edinburgh was a key factor in the evolution of his rebellious attitude toward the Mother Country, for here he was introduced to republican principles by one John Bostock, a fellow medical student. He also was influenced by Catherine Macaulay, an English historian considered

by many contemporaries to be one of the most radical republicans in Great Britain. By January, 1769, Rush held an "exalted opinion" of her "character and principles . . . ."

Upon returning to Philadelphia in 1769, Rush began associating with men whose conversation "daily nourished" those republican principles to which he had been exposed in Edinburgh. Consequently, the doctor's republicanism soon rivaled the most radical detractors of hereditary institutions. Also, Rush's puritanical proclivities prompted his attention to the Calvinist ministers' exhultations for a regeneration of American society. They asserted that the British "tyranny" during the years immediately preceding the Revolution was a divine punishment for the vices (idleness, intemperance, infidelity, pursuit of luxury, etc.) of the American people. Thus America must become, in Samuel Adams' revealing words, "a Christian Sparta." Considering Rush's Calvinistic background and his burgeoning republicanism, he was almost certain to embrace these concepts.

Rush soon became convinced that the adominations of Americans were due to the corrupting influence of British society. As early as 1766 he had condemned the chamber of Parliament as a "cursed haunt of venality, bribery and corruption!" By 1776 Rush was so obsessed with his fear of British influence that in referring to the recently promulgated Declaration of Independence he declared:

> Such inestimable blessings can not be too joyfully received nor purchased at too high a price. They would be cheaply bought at the loss of all the towns & of every fourth, or even third man in America. I tremble to think of the mischiefs that would spread thro' this country had we continued our dependence on Gt Britain twenty years longer. The contest two years ago found us contaminated with British customs manners & ideas of government.

Rush's desire for Independence was matched by his activities to promote its achievement. In 1773 he helped plot a successful resistance to the landing of the British East India Company's tea in Philadelphia and produced propagandistic essays for the patriots' cause: "I wrote under a variety of signatures, by which means an impression of numbers in favor of liberty was made upon the minds of its friends and enemies." Even more important than Rush's own writing activities, however, was his role in the production of Thomas Paine's *Common Sense.*

Rush first encountered Paine at a Philadelphia bookstore, was intrigued by his conversation, and became convinced that Paine's ideas concerning American Independence were similar to his own. Rush had been preparing an essay espousing Independence, but had hesitated, fearing the consequences of its "not being well received." He therefore proposed that Paine write such a pamphlet, and the Englishman readily assented to the idea. As he progressed in his work, Paine visited the doctor at his home and read each chapter to him. Upon completion of the essay, Rush suggested that the author show his work to Benjamin Franklin, David Rittenhouse (the noted astronomer), and Samuel Adams. He also suggested Paine change his proposed title, *Plain Truth,* to *Common Sense;* and in Robert Bell, Rush found a patriotic printer to publish the treasonous tract.

Rush's anti-English sympathies were known to other Pennsylvanians desiring Independence. Consequently, he was elected to the Continental Congress on July 20, 1776, and had taken his seat by July 22. On August 2 the patriotic physician proudly signed the document which he had done much to promote—the Declaration of Independence. Rush had formally and irrevocably committed himself to the Revolution.

For a time Rush expected the exigencies of the Revolution to stimulate a behavioral reformation among Americans, but by the end of the War he realized that the adversities of Revolution had not been sufficient to effect the extensive regeneration he desired. Hence for Rush the Revolution did not end in 1783: "on the contrary, nothing but the first act of the great drama is closed." The formidable task of bringing "the principles, morals, and manners of our citizens" in line with republican institutions remained to be completed.

The Republic of Rush's dream would be

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notable for its domestic tranquility and for its economic prosperity. Its citizens would be renowned for virtue, piety, and patriotism. Vice would be eliminated; especially repugnant to Rush were the sins of idleness and greed. Furthermore, virtually all men would be intelligent voters, knowledgeable on local, state, and national issues. Political parties would not exist, for Americans would endeavor first to serve their country rather than the particular interest of a group or faction.

Rush pursued his mission in a variety of ways. Through public letters, many broadsides, and numerous pamphlets, he propagandized for proper republican governments, for assorted penal reforms (including abolition of capital punishment), and for remarkable educational changes. He also attacked slavery, spirituous liquors, war, tobacco, and other "evils" of American society. All of this was done in addition to his devotion to teaching and practicing medicine. The enormity of his burden led him to exclaim in 1789: "O! for an ocean of health and time!"

Rush's mechanistic psychological theories coupled with humanitarianism stimulated him in these various activities. He believed that men could become good republicans only if exposed to the proper social, educational, and physical environment. Education was a major concern for Rush; indeed, he considered education for all, including women, as an essential ingredient in preparing the masses for republicanism. Hence the doctor designed a model educational system, detailing institutions from kindergartens to a federal university and suggesting curricula and activities that would "convert men into republican machines."

Equally as important as the subject matter to be taught, in Rush's view, was the proper physical regimen. Thus for students he prescribed the following:

> They should live on a temperate diet, consisting chiefly of broths, milk and vegetables. . . . They should also be accustomed occasionally to work with their hands, in the intervals of study, and in the busy seasons of the year in the country. Moderate sleep, silence, occasional solitude and cleanliness should be inculcated upon them, and the utmost advantages should be taken of a proper direction of those great principles in human conduct —sensibility, habit, imitations, and association. The influence of these physical causes will be powerful upon the intellects as well as the principles and morals of young people.

Rush's views toward education were similar to those of Thomas Jefferson, except the Philadelphian stressed that education should implant both patriotism and religion in students. Rush believed religion was necessary to promote virtue and to discourage vice. If children were "carefully instructed in the principles and obligations of the Christian religion," they would become "dutiful children, teachable scholars, and afterwards, good apprentices, good husbands, good wives, honest mechanics, industrious farmers, peaceable sailors, and . . . good citizens."

In addition to education and religion, governmental forms also were a crucial factor in Rush's ideal republic. There was, of course, no place in his conception of republican government for anything that smacked of hereditary institutions. But he did not favor the establishment of a simple or direct democracy; rather, republican government was to strike a middle ground between democracy and monarchy. The ideal republican government would provide "restraints against the tyranny of rulers on the one hand and the licentiousness of the people on the other."

From 1776 until 1790, the Philadelphian persistently promoted the establishment of what he deemed necessary and proper forms of government for both Pennsylvania and the United States. It was in 1790 that the radically democratic Pennsylvania Constitution of 1776 was replaced with a document that met Rush's approval. The state Constitution of 1776 had established Pennsylvania's government as a simple, representative democracy. An assembly elected by universal manhood suffrage held the ultimate power in Pennsylvania—neither the Council (chosen by the Assembly) nor its President were invested with veto power. The Assembly was virtually all powerful.

Rush was equally as ardent in his opposition to the Constitution of 1776 as he was in his support for American Independence. In fact, his *Observations upon the Present Government of Pennsylvania in Four Letters* was the most comprehensive critique of the Pennsylvania Constitution. For Rush, the most objectionable aspect of this docu-

ment was its lack of checks and balances and separation of powers. He believed that "all governments are safe and free in proportion as they are compounded in a certain degree, and . . . all governments are dangerous and tyrannical in proportion as they approach to simplicity." Rush particularly was upset with the Pennsylvania Constitution because the all-powerful legislature was unicameral.

Rush succinctly summarized his criticisms of the Constitution of 1776 in a letter to John Adams in 1779:

> The perfection of government consists in providing restraints against the tyranny of rulers . . . and the licentiousness of the people . . . By our Constitution we are exposed to all the miseries of both without a single remedy for either.

To attack this defective document, Rush became a prominent member of the Republican Party, the membership of which was devoted to reforming or completely replacing the Radicals' Constitution. Supporters of the Constitution formed the Constitutional Party and Pennsylvania's fundamental law became the focal point of a bitter party struggle. The physician and the Republicans finally triumphed in 1790 when Pennsylvania adopted a new constitution.

During the latter half of the 1780's, however, Rush and other Pennsylvanians were caught in a controversy concerning another document—the Federal Constitution of 1787. During the course of the Convention at Philadelphia, Rush heard enough about what was being created so that by August, 1787, he could report that "from the conversation of the members of the convention, there is reason to believe the Federal Constitution will be wise, vigorous, safe, free, and full of dignity." When the Constitution of 1787 was presented to the public, Rush became a leader in the campaign for its ratification in Pennsylvania.

Several factors motivated Rush's ardent support of the Federal Constitution. Extremely important was the fact that the new Constitution became a major issue in Pennsylvania politics. Many of the principles embodied in the Federal Constitution were basically those that the Pennsylvania Republicans had been advocating for Pennsylvania's government for years. Generally speaking, therefore, the Pennsylvania Constitutionalists became Antifederalists and the Republicans became Federalists.

Rush's deep involvement in partisan state politics may be shown by a brief examination of his attitude toward those who supported the radical Constitution of 1776. He considered the Constitutionalists to be "tyrants, fools, and traitors" from whose hands the state had to be rescued by a new Constitution. Indeed, Rush believed that "no man can be of their party and preserve his integrity." Moreover, he was convinced that heaven was on the side of the Republicans; hence there could be no compromise in Rush's opposition to the Radicals.

Rush's bitter opposition to the Pennsylvania Constitution of 1776 and his activities designed to bring about its destruction were well known to his political enemies. Thus the Antifederalist writer "Centinel" asserted that the Pennsylvania Republicans were character assassins and that "Galen" (Rush) "in this barbarous game of policy" had "shone conspicuous beyond all the imps of the well born." Again referring to Rush, "Centinel" noted that "Doctor Puff the paragraphist" was, next to James Wilson, the chief propagandist for the new Constitution. Indeed, the Antifederalist continued, "beneath his pen thousands of correspondents rise into view, who all harmonize in their sentiments and information about the new constitution." "Centinel" also accused Rush of supporting the Federal Constitution because he felt it would lead to the destruction of the Pennsylvania Constitution of 1776.

"Centinel" was correct in linking Rush's support of the Federal Constitution with his desire to destroy his state's constitution. Indeed, Rush asserted that "the new federal government like a new continental wagon will overset our state dung cart with all its dirty contents (reverend & irreverent) and thereby restore order and happiness to Pennsylvania." He was certain that "the new government will demolish our Balloon Constitution. If it had no other merit, this would be enough for me."

Rush was one of five men elected to represent Philadelphia in the Pennsylvania State Ratifying Convention, and he wasted little time in using this forum for attacking the State Constitution of 1776. On the first day the Convention convened, he moved that a minister be obtained to deliver a prayer

upon the opening of the "business of the convention" the next day. This was to avoid a past mistake: "that the convention who framed the government of Pennsylvania, did not preface their business with prayer is probably the reason that the state has ever since been distracted by their proceedings."

Rush's advocacy of the Federal Constitution was not based entirely on partisan motives—he was convinced that it would produce the "freest, purest, and happiest government on the face of the earth" because it incorporated the principles of separation of powers and checks and balances. Hence he approvingly noted that "neither the House of Representatives, the Senate, or the President can perform a single legislative act by themselves." Moreover, he continued, the very nature of man "will lead them to watch, to check, and to oppose each other should an attempt be made by either of them upon the liberties of the people." Rush had been advocating a balanced government for Pennsylvania since 1776.

Another reason that Rush enthusiastically supported the Federal Constitution was his disgust with the weaknesses—both in domestic and foreign affairs—of the national government under the Articles of Confederation. The era of the Confederation was certainly a "critical period" to contemporary American intellectuals, as corruption was felt to be destroying the American Republic as it had the Roman Republic before it. Rush was certainly no exception to this generalization; he saw the period of the Confederation as years of anarchy. Such occurrences as Shays' Rebellion were foreign to the physician's concept of a well-ordered republic.

Rush was gratified with the adoption of the Federal Constitution in 1788 and the promulgation of the Pennsylvania Constitution of 1790, but the decade of the 1790's was one of disillusionment. His involvement in politics had made him a target for aspersions which wounded Rush, who was quite intolerant of criticism. Furthermore, he bitterly opposed the financial policies of Secretary of the Treasury Alexander Hamilton, and he was dismayed with the rise of intense partisan rivalry between the Federalists and the Democratic-Republicans. The rise of Napoleon Bonaparte also dashed Rush's view of the French Revolution as the harbinger of republicanism to Europe. Perhaps just as important as these disappointments, however, was the storm of criticism which descended on Rush for his mode of treating yellow fever and for his assertion that the malady was of domestic origin—criticism which he felt had political overtones.

During the epidemic of 1793, Rush's debilitating methods of treating yellow fever with copious bleedings and heroic purges were attacked by many of his colleagues, but he resolutely stood by his mode of treatment. He likened his situation to that of the "French Republic, surrounded and invaded by new and old enemies. . . ." A few years later, Rush ascribed the opposition to his "remedies . . . chiefly to an unkind and resentful association of my political principles with my medical career."

Rush received the most severe abuse during the latter years of the decade, when Philadelphia was afflicted with an even worse yellow fever outbreak than in 1793. His chief detractor was William Cobbett, an English immigrant aptly described as a "passionate monarchist, whose nostalgia and chauvinism led him to glorify everything English." Using the pen name "Peter Porcupine," Cobbett began publishing *Porcupine's Gazette* in 1797. He castigated individuals such as Lafayette, James Madison, Benjamin Franklin ("Old Lightning Rod"), Thomas Jefferson, and Thomas Paine, but he conserved his best efforts for Benjamin Rush. Rush apparently drew Cobbett's attention by exhibiting his republicanism in a public eulogy for the astronomer David Rittenhouse. His sympathy for the French Revolution also was known, and his controversial yellow fever treatment made him a particularly vulnerable target for Cobbett's vituperation.

Cobbett's attacks were venemous. He opened one article, "Medical Puffing," with the following verse:

> The times are ominous indeed,
> when quack to quack cries purge and bleed.

Cobbett also declared that while the Israelite (Samson) slew his thousands "the Rushites have slain their tens of thousands." "Porcupine's" continual invective finally pro-

voked Rush to sue for libel and the doctor eventually was awarded $5,000, although he collected only a part of it. Cobbett retreated to New York and for a time vindictively produced a small periodical—the *Rush-Light*—solely designed to defame Rush and his supporters. "Porcupine" finally gave up his sport in June, 1800, and sailed for England.

Rush was distressed greatly by this abuse which generated a decline in both his reputation and his practice. In 1798 he acknowledged that he had been forced to borrow money to support his family. In fact he became so discouraged that in 1797 he applied for a professorship at Columbia University and he planned to move if accepted. However, Rush's acceptance at Columbia was blocked by his political enemy, Alexander Hamilton. Rush finally acquired a country villa, "Syndenham," and apparently intended to move there should he be forced to quit Philadelphia.

As with the earlier epidemic, Rush again believed that his political beliefs generated much of the criticism. Thus he asserted to John Dickinson in 1797: "My remedies for the yellow fever would have met with no opposition this year had I not signed the Declaration of Independence and latterly declared myself a Republican in the Eulgium of Mr. Rittenhouse." Rush's idealism was deeply scarred by the disappointments he suffered during the 1790's, but even greater disillusionment followed, for after 1800 he became disenchanted with American society.

Rush had been convinced in 1790 that because of the influence of Quakers and Germans there was "more republicanism" in Philadelphia "than in any other city in the United States." However, during the 1790's the conspicuous consumption of the City's local gentry was augmented by the "social eddies" created by officers of the federal government. By 1809 Rush felt that Philadelphian society had decayed to the point that men who "outroyal in toryism the British nation, the British ministry, and even the British King himself . . . hold in a degree the balance, if not of power, certainly of fashion and character in our city."

The lust for money, which Rush felt Hamilton's system for funding the national debt had engendered, was especially repugnant to him. There was no place in his ideal society for speculators; good republicans were productive and frugal. By 1808 the physician gloomily could assert that the United States was a "bedollared nation." Philadelphia's streets and parlors were "constantly vocal with the language of a broker's office and even at convivial dinners 'Dollars' are a standing dish upon which all feed with rapacity and gluttony." For Rush, "a city in flames kindled by the hand of war" was not "so melancholy a sight as a whole nation absorbed in the love of money. . . ."

Rush also viewed the "worshipping" of George Washington as significant evidence of a corrupted society. In 1798 he complained that "we ascribe all the attributes of the Deity to the name of General Washington." Such adulation was most unrepublican in Rush's eyes. In 1812 he was certain that idolization of Washington was one of the provocations of the "wrath of Heaven to inflict us with this war [of 1812]."

The War of 1812 was interpreted by Rush as the second war for American independence. As England and France continued to "trample upon the rights of individuals and nations" in 1809, Rush became convinced that Americans of the Revolutionary period would have been ready to fight to protect their rights and independence. He imagined that he saw the patriots and heroes of that era standing before him, "some of them just emerging from their graves. . . ." He continued:

> They hear of British and French insults and aggressions and of our dismantled navy and unprotected commerce. They inquire into the conduct and character of the members of the present Congress. . . . They recover the paleness of death in hearing the details of the degeneracy and depravity of the country for which they toiled and bled. Their looks indicate a mixture of grief and indignation. Behold, they tread back their steps and descend with haste and pleasure to their graves. . . .

For Rush a "field of battle covered with dead bodies" was not "so awful a spectacle as a nation deliberately preferring slavery to liberty, and commerce to national independence."

Following the Declaration of War on England, Rush was appalled to observe that many citizens did not support the war effort. The dour doctor dejectedly noted that even among those who were patriotic it was not the same as in 1776. Rush believed that

it would have been "more in unison with our habits and principles, had Congress instead of declaring war sent an advertisement" as follows to be published in European newspapers:

> For Sale
> to the highest bidder
> The United States of America
> Terms of Payment—A bank in every village in the country . . . and a dozen in every city; commerce with the whole world; a whiskey distillery on every farm; and a charter conveying to the whole nation and to every individual in it the title of "Disciples of Washington." . . .

Despite the intense disappointments of his old age, Rush still hoped that his Revolutionary republican dream would someday be realized in the United States. To promote this end, he proposed in 1811 that John Adams leave behind a "posthumous address to the citizens of the United States" which would espouse "all those great national, social, domestic, and religious virtues which alone can make a people free, great, and happy." Rush did not hesitate to mention topics he felt the former president should discuss in his work. His suggestions included stressing: the necessity of religion and public worship, the importance of "early marriage and fidelity to the marriage bed," the desirability of female education, the evils of banks and funding systems, the benefits of free schools, and the ill-effects of "ardent spirits." Rush further noted that he had only "hinted" at a few things Adams should emphasize.

In his twilight years, Rush had become disillusioned with American society, but he had never abandoned his republican ideals of 1776. He always believed that given the proper mixture of active religion, suitable education, social reform, and republican government, a "city upon a hill"—his republican utopia—could be created for the world to observe and to emulate. The republic that he envisoned seems to have been beyond human attainment, and one might be tempted to dismiss Rush as an idealistic dreamer. But this would be a sad mistake, for Rush's role in the creation of *Common Sense* was vital to the cause of Independence, and he promoted acceptance of the Federal Constitution in Pennsylvania. Moreover, he was an important early advocate of such reforms as abolition of slavery, temperance, penal reform, humane and scientific treatment for insanity, and education for women. As a physician in politics, Benjamin Rush certainly left his mark on American society. □

NOTE ON SOURCES

This article was distilled from the author's MA thesis entitled "The Political Thought of Benjamin Rush" which is available at the Oklahoma State University Library. The two sources most heavily relied upon in preparing this article were Lyman H. Butterfield, ed., *The Letters of Benjamin Rush* (2 vols.; Princeton University Press, 1951), and George W. Corner, ed., *The Autobiography of Benjamin Rush: His "Travels Through Life" together with his Commonplace Book for 1789-1813* (Princeton: Princeton University press, 1948.) Another important primary source is Dagobert D. Runes, ed., *The Selected Writings of Benjamin Rush* (New York: The Philosophical Library, Inc., 1946).

Important secondary works used included two biographies of Rush: Carl Binger, *Revolutionary Doctor: Benjamin Rush, 1746-1813* (New York: W. W. Norton & Co., Inc., 1966), and Nathan G. Goodman, *Benjamin Rush: Physician and Citizen, 1746-1813* (Philadelphia: University of Pennsylvania Press, 1934). Other important secondary sources were Harry G. Good, *Benjamin Rush and his Services to American Education* (Berne, Indiana: Witness Press, 1918); David Hawke, *In the Midst of a Revolution* (Philadelphia: University of Pennsylvania Press, 1961); John H. Powell, *Bring Out Your Dead: The Great Plague of Yellow Fever in Philadelphia in 1793* (Philadelphia: University of Pennsylvania Press, 1949); and Gordon S. Wood, *The Creation of the American Republic, 1776-1787* (Chapel Hill: University of North Carolina Press, 1969).

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PROTEIN CONTENT / 1 Cup Prepared Soup*

Bean with Bacon	7.7	Green Pea	7.8
Beef	9.1	Hot Dog Bean	8.6
Chicken Broth	8.4	Oyster Stew	6.0
Chicken 'N Dumplings	6.6	Pepper Pot	6.9
Chili Beef	7.0	Split Pea with Ham	11.6
Consomme	5.6	Vegetable Beef	5.7

When protein is the focal point in your patients' special diets, Campbell's Soups can be a convenient supplementary source of that essential nutrient.

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the 3 phases of Eve



All women are not equal in their endogenous hormonal output. And, while all oral contraceptives are fundamentally effective, they exhibit **differences in their activity levels and estrogen-progestogen ratios that affect different women differently**—in both short and long-term use. Some brands may be insufficient for the woman's needs or else may exceed them.

Searle offers a family of O.C. products that covers the range of women's needs to help you provide the right pill for the right woman at the right time.

References **1.** Editorial: Oral Contraceptives, Which Pill for Which Patient? Patient Care *3*:90-115 (Feb.) 1969 and *4*:135-145 (June 15) 1970 **2.** Greenblatt, R. B.: Progestational Agents in Clinical Practice, Med. Sci. *18*:37-49 (May) 1967 **3.** Kistner, R. W.: Gynecology: Principles and Practice, ed. 2, Chicago, Year Book Medical Publishers, 1971 **4.** Kistner, R. W.: The Pill: Facts and Fallacies About Today's Oral Contraceptives, New York, Delacorte Press, 1968 **5.** Nelson, J. H.: Clinical Evaluation of Side Effects of Current Oral Contraceptives, J. Reprod. Med. *6*:50-55 (Feb.) 1971 **6.** Orr, G. W.: Oral Progestational Agents: Therapy and Complications, S. Dakota J. Med. *22*:11-17 (Jan.) 1969

the Ovulen phase

Most women* with a **balanced hormone profile and normal menses** do best on a middle-of-the-road pill that is neither estrogen dominant nor strongly progestogen dominant.

(*Typical clues—normal body build and breasts, feminine appearance, healthy skin and hair. Vaginal cytology slide—balanced "pink and blue.")

Some women having problems on other O.C.s might do well on Ovulen.

Ovulen has a distinctive hormonal balance that combines moderate estrogenic activity with a slight progestogen dominance. It has an excellent record of patient acceptance.

Ovulen®

Each white tablet contains: ethynodiol diacetate 1 mg./mestranol 0.1 mg.

SEARLE

For brief summary of prescribing information, see following page



the Demulen phase

Many women* who secrete **more estrogen** than most do well on a pill with lower estrogen activity and an increased progestogen overbalance.

(*Typical clues—shorter, plumper, full-breasted, with glowing skin and no wrinkles. Vaginal cytology slide "pink.")

Some women with special conditions that may be aggravated by higher estrogen-activity products may do better on this ratio.

Demulen combines minimal estrogenic activity with a moderate ratio of progestogen overbalance. It is particularly well suited to the young when low-dose (activity) is preferred. Demulen offers little risk of the most potent progestogen side effects; early breakthrough bleeding is often transient.

Demulen®

Each white tablet contains: ethynodiol diacetate 1 mg./ethinyl estradiol 50 mcg
Each pink tablet in Ovulen-28® and Demulen®-28 is a placebo, containing no active ingredients.
Both Ovulen and Demulen are available in 21- and 28-pill schedules.

the Enovid-E phase

Some women* who secrete **less estrogen** than most do best on a pill with a moderate estrogen overbalance.

(*Typical clues—oily complexion, acne, hirsutism, masculinity, flat chest. Vaginal cytology slide—"blue.")

Patients with estrogen deficiency may show:

premenopausal syndrome	intermittent depression
early-cycle bleeding	increased appetite
scanty menses	steady weight gain

vaginal candidiasis

Enovid-E not only provides increased estrogenic activity with low progestogen activity, but also contains the only progestogen that is not antiestrogenic. Therefore it offers less risk of high-dose progestogen side effects.

Enovid-E®

Each tablet contains: norethynodrel 2.5 mg./mestranol 0.1 mg.

Oral contraceptives are complex medications and, after reference to the prescribing information, should be prescribed with discriminating care.

for the 3 phases of Eve:

a family of O.C. products

Ovulen®

Each white tablet contains:
ethynodiol diacetate 1 mg./mestranol 0.1 mg.

Demulen®

Each white tablet contains:
ethynodiol diacetate 1 mg./ethinyl estradiol 50 mcg.

Each pink tablet in Ovulen-28® and Demulen®-28 is a placebo, containing no active ingredients.

Actions—Ovulen and Demulen act to prevent ovulation by inhibiting the output of gonadotropins from the pituitary gland. Ovulen and Demulen depress the output of both the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH).

Special note—Oral contraceptives have been marketed in the United States since 1960. Reported pregnancy rates vary from product to product. The effectiveness of the sequential products appears to be somewhat lower than that of the combination products. Both types provide almost completely effective contraception.

An increased risk of thromboembolic disease associated with the use of hormonal contraceptives has now been shown in studies conducted in both Great Britain and the United States. Other risks, such as those of elevated blood pressure, liver disease and reduced tolerance to carbohydrates, have not been quantitated with precision.

Long-term administration of both natural and synthetic estrogens in subprimate animal species in multiples of the human dose increases the frequency of some animal carcinomas. These data cannot be transposed directly to man. The possible carcinogenicity due to the estrogens can be neither affirmed nor refuted at this time. Close clinical surveillance of all women taking oral contraceptives must be continued.

Indication—Ovulen and Demulen are indicated for oral contraception.

Contraindications—Patients with thrombophlebitis, thromboembolic disorders, cerebral apoplexy or a past history of these conditions, markedly impaired liver function, known or suspected carcinoma of the breast, known or suspected estrogen-dependent neoplasia and undiagnosed abnormal genital bleeding.

Warnings—The physician should be alert to the earliest manifestations of thrombotic disorders (thrombophlebitis, cerebrovascular disorders, pulmonary embolism and retinal thrombosis). Should any of these occur or be suspected the drug should be discontinued immediately.

Retrospective studies of morbidity and mortality conducted in Great Britain and studies of morbidity in the United States have shown a statistically significant association between thrombophlebitis, pulmonary embolism, and cerebral thrombosis and embolism and the use of oral contraceptives. There have been three principal studies in Britain[1-3] leading to this conclusion, and one[4] in this country. The estimate of the relative risk of thromboembolism in the study by Vessey and Doll[3] was about sevenfold, while Sartwell and associates[4] in the United States found a relative risk of 4.4, meaning that the users are several times as likely to undergo thromboembolic disease without evident cause as nonusers. The American study also indicated that the risk did not persist after discontinuation of administration and that it was not enhanced by long-continued administration. The American study was not designed to evaluate a difference between products. However, the study suggested that there might be an increased risk of thromboembolic disease in users of sequential products. This risk cannot be quantitated, and further studies to confirm this finding are desirable.

Discontinue medication pending examination if there is sudden partial or complete loss of vision, or if there is a sudden onset of proptosis, diplopia or migraine. If examination reveals papilledema or retinal vascular lesions medication should be withdrawn.

Since the safety of Ovulen and Demulen in pregnancy has not been demonstrated, it is recommended that for any patient who has missed two consecutive periods pregnancy should be ruled out before continuing the contraceptive regimen. If the patient has not adhered to the prescribed schedule the possibility of pregnancy should be considered at the time of the first missed period.

A small fraction of the hormonal agents in oral contraceptives has been identified in the milk of mothers receiving these drugs. The long-range effect to the nursing infant cannot be determined at this time.

Precautions—The pretreatment and periodic physical examinations should include special reference to the breasts and pelvic organs, including a Papanicolaou smear since estrogens have been known to produce tumors, some of them malignant, in five species of subprimate animals. Endocrine and possibly liver function tests may be affected by treatment with Ovulen or Demulen. Therefore, if such tests are abnormal in a patient taking Ovulen or Demulen, it is recommended that they be repeated after the drug has been withdrawn for two months. Under the influence of progestogen-estrogen preparations preexisting uterine fibromyomas may increase in size. Because these agents may cause some degree of fluid retention, conditions which might be influenced by this factor, such as epilepsy, migraine, asthma, cardiac or renal dysfunction, require careful observation. In breakthrough bleeding, and in all cases of irregular bleeding per vaginam, nonfunctional causes should be borne in mind. In undiagnosed bleeding per vaginam adequate diagnostic measures are indicated. Patients with a history of psychic depression should be carefully observed and the drug discontinued if the depression recurs to a serious degree. Any possible influence of prolonged Ovulen or Demulen therapy on pituitary, ovarian, adrenal, hepatic or uterine function awaits further study. A decrease in glucose tolerance has been observed in a significant percentage of patients on oral contraceptives. The mechanism of this decrease is obscure. For this reason, diabetic patients should be carefully observed while receiving Ovulen or Demulen therapy. The age of the patient constitutes no absolute limiting factor, although treatment with Ovulen or Demulen may mask the onset of the climacteric. The pathologist should be advised of Ovulen or Demulen therapy when relevant specimens are submitted. Susceptible women may experience an increase in blood pressure following administration of contraceptive steroids.

Adverse reactions observed in patients receiving oral contraceptives—A statistically significant association has been demonstrated between use of oral contraceptives and the following serious adverse reactions: thrombophlebitis, pulmonary embolism and cerebral thrombosis.

Although available evidence is suggestive of an association, such a relationship has been neither confirmed nor refuted for the following serious adverse reactions: neuro-ocular lesions, e.g., retinal thrombosis and optic neuritis.

The following adverse reactions are known to occur in patients receiving oral contraceptives: nausea, vomiting, gastrointestinal symptoms (such as abdominal cramps and bloating), breakthrough bleeding, spotting, change in menstrual flow, amenorrhea during and after treatment, edema, chloasma or melasma, breast changes (tenderness, enlargement and secretion), change in weight (increase or decrease), changes in cervical erosion and cervical secretions, suppression of lactation when given immediately post partum, cholestatic jaundice, migraine, rash (allergic), rise in blood pressure in susceptible individuals and mental depression.

Although the following adverse reactions have been reported in users of oral contraceptives, an association has been neither confirmed nor refuted: anovulation post treatment, premenstrual-like syndrome, changes in libido, changes in appetite, cystitis-like syndrome, headache, nervousness, dizziness, fatigue, backache, hirsutism, loss of scalp hair, erythema multiforme, erythema nodosum, hemorrhagic eruption and itching.

The following laboratory results may be altered by the use of oral contraceptives: hepatic function: increased sulfobromophthalein retention and other tests; coagulation tests: increase in prothrombin, Factors VII, VIII, IX and X; thyroid function: increase in PBI and butanol extractable protein bound iodine, and decrease in T^3 uptake values; metyrapone test and pregnanediol determination.

References: 1. Royal College of General Practitioners: Oral Contraception and Thrombo-Embolic Disease, J. Coll. Gen. Pract. *13*:267-279 (May) 1967. **2.** Inman, W. H. W., and Vessey, M. P.: Investigation of Deaths from Pulmonary, Coronary, and Cerebral Thrombosis and Embolism in Women of Child-Bearing Age, Brit. Med. J. *2*:193-199 (April 27) 1968. **3.** Vessey, M. P., and Doll, R.: Investigation of Relation Between Use of Oral Contraceptives and Thromboembolic Disease. A Further Report, Brit. Med. J. *2*:651-657 (June 14) 1969. **4.** Sartwell, P. E.; Masi, A. T.; Arthes, F. G.; Greene, G. R., and Smith, H. E.: Thromboembolism and Oral Contraceptives: An Epidemiologic Case-Control Study, Amer J. Epidem. *90*:365-380 (Nov.) 1969.

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norethynodrel 2.5 mg./mestranol 0.1 mg.

Actions—Enovid-E acts to prevent ovulation by inhibiting the output of gonadotropins from the pituitary gland. Enovid-E depresses the output of both the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH).

Indication—Enovid-E is indicated for oral contraception.

The *Special Note, Contraindications, Warnings, Precautions* and *Adverse Reactions* listed above for Ovulen and Demulen are applicable to Enovid-E and should be observed when prescribing Enovid-E.

SEARLE **Enovid-E®**

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Where "The Pill" Began

Books As Clinical Tools

Annotated Book List For Practicing Physicians (1972)

KELLY M. WEST, MD
RUTH W. WENDER, MLS*

One of the purposes of these columns has been to provide for practicing physicians up-to-date information about the characteristics and quality of those books which have greatest relevance to the day to day problems of clinical practice. Another purpose of providing such information is to assist hospitals in making the best possible use of their limited budgets for library services. The most recent of our lists of recommended books appeared in 1971.[1] The most gratifying responses to these previous lists have come from small hospitals which do not have professional librarians to supervise their programs of acquisition. Our previous columns have also called attention to the several other very helpful lists which have appeared from time to time. The list of books and journals developed under the supervision of Brandon appeared most recently in April of 1971.[2] It includes 389 well-selected book titles. An excellent smaller core list of books has been prepared and issued from time to time by Stearns and his associates.[3] Finally there is available a relatively comprehensive list of medical books which is issued periodically by the F. A. Majors Company.[4] Most of the offerings of the major companies are on this list, but a small percentage of important books are not listed for various reasons. This would include, for example, some of the books published abroad and those issued by special groups such as the American Diabetes Association. The Majors list contains hundreds of volumes, and no attempt is made to be selective.

The excellent lists of Brandon and Stearns are intended to serve the broad needs of hospital personnel, including nurses, laboratory technicians, and other health professionals. These lists also give more attention to representative books in the basic medical sciences. The publications of Brandon and Stearns also provide very useful advice and references relating to the establishment and operation of a small hospital library. Our list, on the other hand, is developed especially to meet the needs of the practicing physician. Many excellent books are not in our list, usually because they are either: (a) highly specialized, (b) concerned mainly with basic or clinical science rather than clinical practice, or (c) they were published prior to 1966. A major purpose of our list is to provide information on books published in recent months. Many useful books on this 1972 list were not on any of the lists published prior to 1972. We understand that the brief annotations which were a part of our 1971 list have been useful to some of the

One of a series sponsored by the Department of Continuing Education, University of Oklahoma College of Medicine.
*Coordinator, Library and Information Services Project, Oklahoma Regional Medical Program, University of Oklahoma Health Sciences Center Library.

hospitals and physicians. The subject headings used in the other lists referred to above conform more suitably to standard library practices. Our subject headings are arranged using a clinical frame of reference which practitioners have found helpful. The list of 254 books follows:

REFERENCES

1. West, K. M. and Wender, R. W.: Books as Clinical Tools, An Annotated Book List for Physicians. J. Okla. Med. Assn., 64: 100-108, Mar. 1971.
2. Brandon, Alfred N.: Selected List of Books and Journals for the Small Medical Library. Bull. Med. Libr. Assn., 59: 267-285, April, 1971.
3. Stearns, Norman S., and Ratcliff, Wendy W.: An Integrated Health-Science Core Library for Physicians, Nurses, and Allied Health Practitioners in Community Hospitals. New Eng. J. Med., 283: 1489-1498, December 31, 1970.
4. A Select List of Medical Books in Print—1972. City of Industry, California, J. W. Stacey, 1972. (Available through most medical book stores, major medical publishers, and outlets of J. A. Majors Co., such as the one in Dallas, 8911 Directors Row, P.O. Box 47552.)

THE LIST

ACID-BASE BALANCE (See fluids and electrolytes)

ALLERGY AND IMMUNOLOGY

Criep, L. H.: *Clinical Immunology and Allergy*. 2d ed. New York, Grune & Stratton, 1969. $35.50.

Freedman, S. O.: *Clinical Immunology*. New York, Harper & Row, 1971. $20.00

Gell, P., and Coombs, R. R. A. (Editors): *Clinical Aspects of Immunology*. 2d ed. Philadelphia, Davis, 1968. $26.00.

Samter, M. (Editor): *Immunological Diseases*. 2d ed. Boston, Little, Brown, 1971. 2 vols. $45.00.

Sheldon, J. M., *et al: A Manual of Clinical Allergy*. 2d ed. Philadelphia, Saunders, 1967. $16.00.

Comment: The book of the late John Sheldon and his associates published in 1967 is slightly out of date in a few respects. But it is a very good short book on clinical allergy and probably the best bargain available for non-allergists. Samter's book is much larger and more comprehensive. Published in 1971, it is an excellent reference source, although somewhat expensive ($45.00).

ANATOMY (See surgery)

ANESTHESIOLOGY

Collins, V. J.: *Principles of Anesthesiology*. Philadelphia, Lea & Febiger, 1966. $35.00.

Dripps, R. D., *et al.: Introduction to Anesthesia*. 3d ed. Philadelphia, Saunders, 1967. $10.50.

Wylie, W. D., and Churchill-Davidson, H. C.: *A Practice of Anesthesia*. 3d ed. Chicago, Year Book, 1971. $35.00.

Comment: Probably the best general reference source is the book of Wylie. The book of Collins is also good and covers similar ground. The book of Dripps is smaller, cheaper, and more elementary. Physicians who are not anesthesiologists will find it a helpful volume.

ARTHRITIS AND RHEUMATISM

Copeman, W. S. C.: *Textbook of the Rheumatic Diseases*. 4th ed. Baltimore, Williams & Wilkins, 1969. $36.00.

Hollander, J. L. (Editor): *Arthritis and Allied Conditions; a Textbook of Rheumatology*. 8th ed. Philadelphia, Lea & Febiger, 1972. In Preparation.

Comment: Hollander's book is our first choice.

CANCER

Ackerman, L. V., and Del Regato, J. A.: *Cancer: Diagnosis, Treatment, and Prognosis*. 4th ed. St. Louis, Mosby, 1970. $41.50.

Cline, M. J.: *Cancer Chemotherapy*. Philadelphia, Saunders, 1971. $10.00.

Cole, W. H. (Editor): *Chemotherapy of Cancer*. Philadelphia, Lea & Febiger, 1970. $12.50.

Moore, C.: *Synopsis of Clinical Cancer*. 2d ed. St. Louis, Mosby, 1970. $11.75.

Comment: Our first choice is the book of Ackerman and Del Regato. Note that it is fairly expensive ($41.50). Although not as comprehensive, the small inexpensive book of Moore is also good. There are several books on chemotherapy. Cline's book is quite recent, an important consideration in this rapidly changing field. It is relatively brief and elementary in its treatment of certain aspects, and therefore of less utility for the specialist in this field. But it is a good reference for physicians who are not oncologists. The book edited by Cole is also good, and relatively recent (1970).

CARDIOVASCULAR DISEASES (See also pulmonary diseases for thoracic surgery)

Bellet, S.: *Clinical Disorders of the Heart Beat*. 3d ed. Philadelphia, Lea & Febiger, 1971. $52.50.

Burch, G. E.: *A Primer of Cardiology*. 4th ed. Philadelphia, Lea & Febiger, 1971. $9.50.

Chung, E. K. (Editor): *Principles of Cardiac Arrhythmias*. Baltimore, Williams & Wilkins, 1971. $24.75.

Conn, H. L., Jr., and Horwitz, O. (Editors): *Cardiac and Vascular Diseases*. Philadelphia, Lea & Febiger, 1971. 2 vols. $39.50.

Fairbairn, J. F., II, *et al.* (Editors): *Peripheral Vascular Disease*. 4th ed. Philadelphia, Saunders, 1972. $27.50.

Fowler, N. O.: *Cardiac Diagnosis*. New York, Harper & Row, 1968. $23.50.

Friedberg, C. K.: *Diseases of the Heart*. 3d ed. Philadelphia, Saunders, 1966. $22.00.

Hurst, J. W., and Logue, R. B.: *The Heart: Arteries and Veins*. 2d ed. New York, McGraw-Hill, 1970. $32.50.

Meltzer, L., *et al.: Intensive Coronary Care*. Philadelphia, Charles Press, 1968. $6.00.

Oram, S.: *Clinical Heart Disease*. Philadelphia, Davis, 1971. $42.00.

Pickering, G.: *High Blood Pressure*. 2d ed. New York, Grune & Stratton, 1968. $18.00.

Stephenson, H. E.: *Cardiac Arrest and Resuscitation*. 3d ed. St. Louis, Mosby, 1969. $29.50.

Toole, J. F., *et al.: Cerebral Vascular Disease*. New York, Grune & Stratton, 1971. $9.75.

Wood, P. H.: *Diseases of the Heart and Circulation*. 3d ed. Philadelphia, J. B. Lippincott, 1968. $29.00.

Comment: Of the more comprehensive texts, both Wood and Friedberg are excellent. They are not, however, as recent as some of the other books. Probably the best general reference source now is the book edited by Hurst and Logue. The British book of Oram is also good. The volumes edited by Conn

and Horwitz are well done. (There have been many recent books concerning coronary care and the arrhythmias.) Not all of the recent publications are listed here. Probably the most comprehensive volume on the arrhythmias is the third edition of the book of Bellet. This, however, is expensive ($52.50). The best general volume on peripheral vascular diseases is the recent publication of Fairbairn and associates. This book is the successor to the book which had been written by Allen, Barker, and Hines.

DERMATOLOGY

Andrews, G. C., and Domonkos, A. N.: *Diseases of the Skin.* 6th ed. Philadelphia, Saunders, 1971.

Fitzpatrick, T. B., *et al.* (Editors): *Dermatology in General Medicine.* New York, McGraw-Hill, 1971. $42.50.

Pillsbury, D. M.: *A Manual of Dermatology.* Philadelphia, Saunders, 1971. $15.00.

Rook, A., *et al.* (Editors): *Textbook of Dermatology.* 2d ed. Philadelphia, F. A. Davis, 1968. 2 vols. $69.00.

Stewart, W. D., *et al.: Synopsis of Dermatology.* 2d ed. St. Louis, Mosby, 1970. $13.85.

Comment: For dermatologists, the very comprehensive volumes edited by Rook and associates are probably the best source of information. Note, however, that this publication is expensive ($69.00). Our first choice of the smaller volumes is the new edition of Pillsbury. The recent edition of Andrews and Domonkos is one of the better dermatology books.

DIAGNOSIS

Barondess, J. A.: *Diagnistic Approaches to Presenting Syndromes.* Baltimore, Williams & Wilkins, 1971. $21.50.

Bauer, J.: *Differential Diagnosis of Internal Diseases.* 3d ed. New York, Grune & Stratton, 1966. $34.00.

Cope, Z.: *The Early Diagnosis of the Acute Abdomen.* 13th ed. New York, Oxford University Press, 1968. $6.00.

Douthwaite, A. H. (Editor): *French's Index of Differential Diagnosis.* 9th ed. Baltimore, Williams & Wilkins, 1967. $25.50.

Harvey, A. M., and Bordley, J.: *Differential Diagnosis; the Interpretation of Clinical Evidence.* 2d ed. Philadelphia, Saunders, 1970. $27.00.

MacBryde, C. M., and Blacklow, R. S. (Editors): *Signs and Symptoms; Applied Pathologic Physiology and Clinical Interpretation.* 5th ed. Philadelphia, Lippincott, 1970. $22.50.

Comment: Our current preferences are for the books of Harvey and of MacBryde.

DIETETICS (See nutrition)

DRUGS (See pharmacology and therapeutics)

ELECTROCARDIOGRAPHY (See cardiovascular diseases)

ELECTROLYTES (See fluids and electrolytes)

EMERGENCIES (See also cardiovascular diseases, orthopedics, pharmacology and therapeutics [poisoning], surgery, and others)

Birch, C. A. (Editor): *Emergencies in Medical Practice.* 9th ed. Baltimore, Williams & Wilkins, 1971. $19.75.

Brooks, D. K.: *Resuscitation.* Baltimore, Williams & Wilkins, 1967. $13.00.

Cole, W. H. and Puestow, C. B.: *Emergency Care: Surgical and Medical.* 7th ed. New York, Appleton, 1972. $12.00.

Eckert, C. (Editor): *Emergency-Room Care.* 2d ed. Boston, Little, Brown, 1971. Paper $9.50, Cloth $14.00.

Flint, T., and Cain, H. D.: *Emergency Treatment and Management.* 4th ed. Philadelphia, Saunders, 1970. $11.50.

Henderson, J.: *Emergency Medical Guide.* 2d ed. New York, McGraw-Hill, 1969. $8.95.

Schneewind, J. H. (Editor): *Medical and Surgical Emergencies.* 2d ed. Chicago, Year Book, 1968. $6.50.

Comment: At present Flint and Cain is our first choice.

ENDOCRINOLOGY AND METABOLISM

Bondy, P. K. (Editor): *Duncan's Diseases of Metabolism: Detailed Methods of Diagnosis and Treatment.* 6th ed. Philadelphia, Saunders, 1969. 2 vols. $39.00.

Ellenberg, M., and Rifkin, H. (Editors): *Diabetes Mellitus; Theory and Practice.* New York, McGraw-Hill, 1970. $35.00.

Fajans, S. S., and Sussman, K. (Editors): *Diabetes Mellitus: Diagnosis and Treatment.* Volume III. New York, American Diabetes Association, 1971. $5.75.

Marble, A., *et al.* (Editors): *Joslin's Diabetes Mellitus.* 11th ed. Philadelphia, Lea & Febiger, 1971. $32.50.

Schneeberg, N. G.: *Essentials of Clinical Endocrinology.* St. Louis, Mosby, 1970. $22.50.

Stanbury, J. B.: *The Metabolic Basis of Inherited Disease.* 3d ed. New York, McGraw-Hill, 1972. $45.00.

Turner, C. D., and Bagnara, J. T.: *General Endocrinology.* 5th ed. Philadelphia, Saunders, 1971. $11.00.

Werner, S., *et al.* (Editors): *The Thyroid.* 3d ed. New York, Harper & Row, 1971. $33.50.

Williams, R. H. (Editor): *Textbook of Endocrinology.* 4th ed. Philadelphia, Saunders, 1968. $24.00.

Comment: The book edited by Bondy is excellent. The volume edited by Williams has been the standard text in endocrinology. It is now in some respects slightly out of date, but still quite useful. The new edition of the book of Stanbury is good. The books on diabetes edited by Marble and by Ellenberg are both quite good. They are comprehensive and somewhat expensive. The smaller volume edited by Fajans and Sussman is recent, quite inexpensive and of excellent quality. Werner's book on thyroid disease is excellent.

EYE DISEASE (See ophthalmology)

FLUIDS AND ELECTROLYTES

Black, D.: *Essentials of Fluid Balance.* 4th ed. Oxford, Blackwell Scientific, 1968. $5.50.

Filley, G. F.: *Acid-Base and Blood Gas Regulation: For Medical Students Before and After Graduation.* Philadelphia, Lea & Febiger, 1971. $10.50.

Goldberger, E.: *A Primer of Water, Electrolyte and Acid-Base Syndromes.* 4th ed. Philadelphia, Lea & Febiger, 1970. $8.50.

Masoro, E. J., and Siegel, P. D.: *Acid-Base Regulation: Its Physiology and Pathophysiology.* Phila-

delphia, Saunders, 1971. $7.50.

Maxwell, M. H., and Kleeman, C. R.: *Clinical Disorders of Fluid and Electrolyte Metabolism.* 2d ed. New York, McGraw-Hill, 1972. $27.50.

Welt, L. G.: *Clinical Disorders of Hydration and Acid-Base Equilibrium.* 3d ed. Boston, Little, Brown, 1972. In preparation.

Comment: The books of Welt, Filley, Masoro, and Maxwell are all recent and well done.

GASTROENTEROLOGY

Bockus, H. L., *et al.: Gastroenterology.* 2d ed. Philadelphia, Saunders, 1963-65. Vol. 1, $26.00; Vol. 2, $29.00; Vol. 3, $31.00. (3 vols. $83.00).

Jones, F. A., *et al.: Clinical Gastroenterology.* 2d ed. Philadelphia, Davis, 1968. $21.50.

Paton, A.: *Liver Disease.* Philadelphia, Lippincott, 1970. $7.25.

Paulson, M. (Editor): *Gastroenterologic Medicine.* Philadelphia, Lea & Febiger, 1969. $60.00.

Schiff, L. (Editor): *Diseases of the Liver.* 3d ed. Philadelphia, Lippincott, 1969. $39.50.

Sherlock, S.: *Diseases of the Liver and Biliary System.* 4th ed. Philadelphia, Davis, 1968. $18.50.

Spiro, H. M.: *Clinical Gastroenterology.* New York, Macmillan, 1970. $35.00.

Truelove, S. C., and Reynell, P. C.: *Diseases of the Digestive System.* 2d ed. Philadelphia, Davis, 1971. $23.50.

Comment: The volumes edited by Bockus are now somewhat out of date in certain respects, but they are still useful sources of information. Among the more recent general textbooks on gastroenterology which are listed above, we have no strong preference. In one of our small core clinical collections in the University Hospital, we have the book of Spiro.

GENETICS (See endocrinology and metabolism)

GYNECOLOGY AND OBSTETRICS

Barnes, C. G.: *Medical Disorders in Obstetric Practice.* 3d ed. Philadelphia, Davis, 1970. $14.00.

Benson, R. C.: *Handbook of Obstetrics and Gynecology.* 4th ed. Los Altos, Lange Medical Publications, 1971. $6.50.

Danforth, D. N. (Editor): *Textbook of Obstetrics and Gynecology.* 2d ed. New York, Harper & Row, 1971. $35.00.

Green, T. H., Jr.: *Gynecology: Essentials of Clinical Practice.* 2d ed. Boston, Little, Brown, 1971. Paperback $9.50. Clothbound $14.00.

Greenhill, J. P.: *Office Gynecology.* 9th ed. Chicago, Year Book, 1971. $21.50.

Hellman, L. M., and Pritchard, J. A. (Editors): *Williams' Obstetrics.* 14th ed. New York, Appleton, 1971. $23.50.

Kistner, R. W.: *Gynecology: Principles and Practice.* 2d ed. Chicago, Year Book, 1971. $23.95.

Macdonald, R. R.: *Scientific Basis of Obstetrics and Gynecology.* Baltimore, Williams & Wilkins, 1971. $19.75.

McLennan, C. E.: *Synopsis of Obstetrics.* St. Louis, Mosby, 1970. $10.25.

Moir, J. C., and Myerscough, P. R. (Editors): *Munro Kerr's Operative Obstetrics.* 8th ed. Baltimore, Williams & Wilkins Co., 1971. $26.25.

Novak, E. R., *et al.* (Editors): *Textbook of Gynecology.* 8th ed. Baltimore, Williams & Wilkins, 1970. $22.50.

Philipp, E. E., *et al.* (Editors): *Scientific Foundations of Obstetrics and Gynecology.* Philadelphia, Davis, 1970. $30.00.

Taylor, E. S.: *Beck's Obstetrical Practice.* 9th ed. Baltimore, Williams & Wilkins, 1971. $19.75.

Taylor, E. S.: *Essentials of Gynecology.* 4th ed. Philadelphia, Lea & Febiger, 1969. $17.00.

Te Linde, R., and Mattingley, R. F.: *Operative Gynecology.* 4th ed. Philadelphia, Lippincott, 1970. $35.00.

Willson, J. R., *et al.: Obstetrics and Gynecology.* 4th ed. St. Louis, Mosby, 1971. $19.80.

Willson, J. R. (Reviser): *Management of Obstetric Difficulties.* 6th ed. St. Louis, Mosby, 1961. $19.50.

Comment: Of the books which cover both obstetrics and gynecology we prefer Danforth. There are several good books in both obstetrics and in gynecology. Of the general books in gynecology we currently favor Novak. In obstetrics, the books of Taylor and of Hellman (formerly Eastman) are well accepted standards.

HEMATOLOGY

Britton, C. J. C. (Editor): *Whitby's Disorders of the Blood: Diagnosis, Pathology, Treatment, Technique.* 10th ed. New York, Grune & Stratton, 1969. $19.75.

deGruchy, G. C.: *Clinical Haematology in Medical Practice.* 3d ed. Philadelphia, Davis, 1970. $16.00.

Eastham, R. D. (Editor): *Clinical Haematology.* 3d ed. Baltimore, Williams & Wilkins, 1970. $7.50.

Leavell, B. S., and Thorup, O. A.: *Fundamentals of Clinical Hematology.* 3d ed. Philadelphia, Saunders, 1971. $18.00.

Williams, W. J., *et al.: Hematology.* New York, McGraw-Hill, 1972. $32.50.

Wintrobe, M. M.: *Clinical Hematology.* 6th ed. Philadelphia, Lea & Febiger, 1967. $22.50.

Comment: For several years the most widely used book has been that of Wintrobe. It is now slightly out of date in some respects. Of the smaller volumes, the book of Leavell and Thorup is good. One of the newest books is the one by Williams and his associates. The British books of deGruchy and Eastham are good and up-to-date.

HEART (See cardiovascular diseases)

IMMUNOLOGY (See allergy and immunology)

INFECTIOUS DISEASES (See also pediatrics and and pharmacology and therapeutics)

American Hospital Association: *Infection Control in the Hospital.* Chicago, A.H.A., 1970. $4.00.

Beck, J. W., and Barrett-Conner, E.: *Medical Parasitology.* St. Louis, Mosby, 1971. $10.75.

Benenson, A. S. (Editor): (American Public Health Association) *Control of Communicable Diseases in Man.* 11th ed. New York, American Public Health Association, 1970. $2.00.

Blair, J. E., *et al.* (Editors): *Manual of Clinical Microbiology.* Baltimore, Williams & Wilkins, 1970. Cloth $12.00, paper $7.00.

Bodily, H. L.: *Diagnostic Procedures for: Bacterial, Mycotic and Parasitic Infections.* 5th ed. New

York, American Public Health Association, 1970. $15.50.

Conant, N. F., *et al.: Manual of Clinical Mycology.* 3d ed. Philadelphia, Saunders, 1971. $13.50.

Debre, R., and Celers, J. (Editors): *Clinical Virology: Evaluation and Management of Human Viral Infections.* Philadelphia, Saunders, 1970. $38.00.

Emmons, C. W., *et al.: Medical Mycology.* 2d ed. Philadelphia, Lea & Febiger, 1970. $16.50.

Faust, E. C., *et al.: Craig and Faust's Clinical Parasitology.* 8th ed. Philadelphia, Lea & Febiger, 1970. $25.50.

Jawetz, E., *et al.: Review of Medical Microbiology.* 9th ed. Los Altos, Lange, 1970. $7.50.

Kagan, B. M.: *Antimicrobial Therapy.* Philadelphia, Saunders, 1970. $14.50.

Smith, H.: *Antibiotics in Clinical Practice.* Baltimore, Williams & Wilkins, 1969. $11.75.

Swain, R. H., and Dodds, T. C.: *Clinical Virology.* Baltimore, Williams & Wilkins, 1967. $16.00.

Top, F. H.: *Communicable and Infectious Diseases: Diagnosis, Prevention, Treatment.* 7th ed. St. Louis, Mosby, 1972. In Preparation.

Comment: Probably the most generally useful book is that of Top because of its broad coverage. Other books listed here contain information in greater depth with regard to certain aspects of infectious disease.

INTERNAL MEDICINE (General)

Beeson, P. B., and McDermott, W. (Editors): *Cecil-Loeb Textbook of Medicine.* 13th ed. Philadelphia, Saunders, 1971. 1 vol. ed. $26.00, 2 vol. ed. $30.00.

Davidson, S., and Macleon, J.: *The Principles and Practice of Medicine.* 10th ed. Baltimore, Williams & Wilkins, 1971. $16.00.

Frohlich, E. D., *et al.* (Editors): *Pathophysiology, Altered Regulatory Mechanisms.* Philadelphia, Lippincott, 1971. $21.00.

Harvey, A. M., *et al.* (Editors): *Principles and Practice of Medicine.* 17th ed. New York, Appleton, 1968. $22.50.

Hunter, G. W., *et al.: A Manual of Tropical Medicine.* 4th ed. Philadelphia, Saunders, 1966. $22.50.

Keefer, C. F., and Wilkins, R. W. (Editors): *Medicine: Essentials of Clinical Practice.* Boston, Little, Brown, 1970. Paper, $11.50, cloth, $18.00.

Krupp, M. A., and Chatton, M. J. (Editors): *Current Diagnosis and Treatment.* rev. ed. Los Altos, Lange, 1972. $11.00.

McCombs, R. P.: *Fundamentals of Internal Medicine: A Physiologic and Clinical Approach to Disease.* 4th ed. Chicago, Year Book, 1971. $17.50.

Mann, W. N., and Lessof, M. H. (Editors): *Conybeare's Textbook of Medicine.* 15th ed. Baltimore, Williams & Wilkins, 1970. $20.75.

Wintrobe, M. M., *et al.* (Editors): *Harrison's Principles of Internal Medicine.* 6th ed. New York, McGraw-Hill, 1970. 1 vol. ed. $26.50, 2 vol. ed. $30.50.

Comment: The two standards are still Beeson and McDermott (Cecil-Loeb) and Wintrobe (Harrison's book).

KIDNEY DISEASE (See also urology)

DeWardener, H. E.: *The Kidney.* 3d ed. Baltimore, Williams & Wilkins, 1968. $16.00.

Hamburger, J., *et al.* (Translated by Walsh, A.): *Nephrology.* Philadelphia, Saunders, 1968. 2 vols. $50.00.

Papper, S.: *Clinical Nephrology.* Boston, Little, Brown, 1971. $16.00.

Strauss, M. B., and Welt, L. G. (Editors): *Diseases of the Kidney.* 2d ed. Boston, Little, Brown, 1971 2 vols. $50.00.

Comment: The book of Strauss and Welt is recent, comprehensive, and outstanding. Of the less expensive and shorter reference books, we prefer the new publication of Papper.

LABORATORY MEDICINE (See also pathology)

Bennington, J. L., *et al.: Laboratory Diagnosis.* New York, Macmillan, 1970. $10.95.

Davidsohn, I., and Henry, J. B. (Editors): *Todd-Sanford Clinical Diagnosis by Laboratory Methods.* 14th ed. Philadelphia, Saunders, 1969. $24.00.

Frankel, S., *et al.* (Editors): *Gradwohl's Clinical Laboratory Methods and Diagnosis: a Textbook on Laboratory Procedures and Their Interpretation.* 7th ed. St. Louis, Mosby, 1970. 2 vol. $62.50.

Goodale, R. H., and Widmann, F. K.: *Clinical Interpretation of Laboratory Tests.* 6th ed. Philadelphia, Davis, 1969. $11.50.

Hoffman, W. S. (Editor): *The Biochemistry of Clinical Medicine.* 4th ed. Chicago, Year Book, 1970. $15.75.

Koepke, J. A.: *Guide to Clinical Laboratory Diagnosis.* New York, Appleton, 1969. $6.75.

Levinson, S. A., and MacFate, R. P. (Editors): *Clinical Laboratory Diagnosis.* 7th ed. Philadelphia, Lea & Febiger, 1969. $28.50.

Miller, S. E., and Weller, J. M. (Editors): *Textbook of Clinical Pathology.* 8th ed. Baltimore, Williams & Wilkins, 1971. $19.50.

Thompson, R. H. S., and Wootton, I. D. P. (Editors): *Bio-chemical Disorders in Human Disease.* 3d ed. New York, Academic, 1970. $28.00.

Wallach, J.: *Interpretation of Diagnostic Tests.* Boston, Little, Brown, 1970. paper, $6.95.

Comment: There are a large number of publications in this field, including some good ones which aren't listed here. Of the several standard general texts on this subject, we prefer the book of Davidsohn and Henry. Several physicians have told us that the inexpensive little book of Wallach has been useful.

LUNG (See pulmonary diseases)

MEDICINE (See internal medicine)

METABOLISM (See endocrinology and metabolism)

MICROBIOLOGY (See infectious diseases)

NEUROLOGY AND NEUROSURGERY

Alpers, B. J., and Mancall, E. L.: *Clinical Neurology.* 6th ed. Philadelphia, Davis, 1971. $35.00.

Baker, A. B., and Baker, L. H.: *Clinical Neurology.* New York, Harper & Row, 1971, 3 looseleaf volumes. $175.00.

Grinker, R. R., and Sahs, A. L.: *Neurology.* 6th ed. Springfield, Illinois, Thomas, 1966. $33.50.

Kahn, E. A., *et al.: Correlative Neurosurgery.* 2d ed. Springfield, Illinois, Thomas, 1969. $31.50.

Kempe, L. G.: *Operative Neurosurgery, Vol. I: Cran-*

ial, Cerebral, and Vascular Disease. New York, Springer, 1968. $39.50.

Kempe, L. G.: *Operative Neurosurgery, Vol. II: Posterior Fossa, Spinal Cord, and Peripheral Nerve Disease.* New York, Springer, 1971. $48.40.

Logue, V. (Editor): *Neurosurgery* (Operative Surgery Ser., Vol. 14) 2d ed. Philadelphia, Lippincott, 1971. $20.00.

Merritt, H. H.: *A Textbook of Neurology.* 4th ed. Philadelphia, Lea & Febiger, 1967. $15.00.

Walshe, F. M. R.: *Diseases of the Nervous System.* 11th ed. Baltimore, Williams & Wilkins, 1970. $14.75.

Walton, J. N. (Editor): *Brain's Diseases of the Nervous System.* 7th ed. New York, Oxford, 1969. $19.50.

Comment: There are many good general textbooks in neurology. We have no strong preference among the general neurology textbooks listed here. The publication edited by the Bakers is too expensive for some purposes ($175.00), but it is an excellent source of detailed information. Of the neurosurgery books we prefer Kahn as a source of information for physicians who are not neurosurgeons.

NUCLEAR MEDICINE (See radiology)

NUTRITION

Davidson, S., and Passmore, R.: *Human Nutrition and Dietetics.* 4th ed. Baltimore, Williams & Wilkins, 1969. $21.50.

Mayo Clinic: *Diet Manual.* 4th ed. Philadelphia, Saunders, 1971. $5.95.

Wohl, M. G., and Goodhart, R. S.: *Modern Nutrition in Health and Disease; Dietotherapy.* 4th ed. Philadelphia, Lea & Febiger, 1968. $30.00.

Comment: The books of Wohl and of Davidson are the best general textbooks available for the clinician.

OBSTETRICS (See gynecology and obstetrics)

ONCOLOGY (See cancer)

OPHTHALMOLOGY

Allen, J. H. (Editor): *May's Manual of the Diseases of the Eye.* 24th ed. Baltimore, Williams & Wilkins, 1968. $9.75.

Newell, F. W.: *Ophthalmology: Principles and Concepts.* 2d ed. St. Louis, Mosby, 1969. $16.75.

Scheie, H. G., and Albert, D. M. (Editors): *Adler's Textbook of Ophthalmology.* 8th ed. Philadelphia, Saunders, 1969. $17.50.

Vaughn, D., *et al.: General Ophthalmology.* 6th ed. Los Altos, Lange, 1971. $8.00.

Comment: For the non-ophthalmologist, our first choice would be Newell, but each of the four volumes listed above are good general reference. We did not list the many volumes edited by Duke-Elder. This excellent series contains very detailed information, much of which would be of interest only to the ophthalmologist. Acquiring all of these would require an investment of more than $400.00.

ORTHOPEDICS

Adams, J. C.: *Outline of Orthopaedics.* 7th. ed. Baltimore, Williams & Wilkins, 1971. $11.75.

Aegerter, E. E., and Kirkpatrick, J. A., Jr.: *Orthopedic Diseases: Physiology, Pathology, Radiology.* 3d ed. Philadelphia, Saunders, 1968. $23.00.

Crenshaw, A. H. (Editor): *Campbell's Operative Orthopaedics.* 5th ed. St. Louis, Mosby, 1971. 2 vols. $79.50.

DePalma, A. F.: *The Management of Fractures and Dislocations: an Atlas.* 2d ed. Philadelphia, Saunders, 1970. 2 vols. $52.00.

Lichtenstein, L.: *Diseases of Bone and Joints.* St. Louis, Mosby, 1970. $18.50.

O'Donoghue, D. H.: *Treatment of Injuries to Athletes.* 2nd ed. Philadelphia, Saunders, 1970. $22.00.

Ralston, E. L.: *Handbook of Fractures.* St. Louis, Mosby, 1967. $13.75.

Raney, R. B., *et al: Shands' Handbook of Orthopaedic Surgery.* 8th ed. St. Louis, Mosby, 1971, $15.00.

Ring, P. A.: *The Care of the Injured.* 2d ed. Baltimore, Williams & Wilkins, 1969. $6.75.

Turek, S. L.: *Orthopaedics: Principles and Their Application.* 2d ed. Philadelphia, Lippincott, 1967. $27.00.

Comment: For the orthopedist, one of the most generally useful reference sources will be the publication of Crenshaw. One of the best sources of information for physicians who are not orthopedists will be the relatively inexpensive ($15.00) book of Raney, *et al.*

OTORHINOLARYNGOLOGY

Ballenger, H. C., *et al.: Diseases of the Nose, Throat, and Ear.* 11th ed. Philadelphia, Lea & Febiger, 1969. $32.50.

DeWeese, D. D., and Saunders, W. H.: *Textbook of Otolaryngology.* 3d ed. St. Louis, Mosby, 1968. $14.00.

Comment: We have no strong preference here. A publication edited by Maloney is not listed here because this excellent series of five volumes is mainly of interest to the otorhinolaryngologists, and it is rather expensive ($148.00).

PATHOLOGY (See also laboratory medicine)

Ackerman, L. V., and Butcher, H. R.: *Surgical Pathology.* 4th ed. St. Louis, Mosby, 1968. $29.75.

Anderson, W. A. D.: *Pathology.* 6th ed. St. Louis, Mosby, 1971. 2 vols. $29.50.

Boyd, W.: *A Textbook of Pathology.* 8th ed. Philadelphia, Lea & Febiger, 1970. $20.00.

Brunson, J. G., and Gall, E. A. (Editors): *Concepts of Disease.* New York, Macmillan, 1971. $23.95.

Florey, H. W. (Editor): *General Pathology.* 4th ed. Philadelphia, Saunders, 1970. $24.00.

Robbins, S. L.: *Pathology.* 3d ed. Philadelphia, Saunders, 1967. $20.50.

Comment: All of the volumes listed above are good general reference books. We have no strong preference among these.

PEDIATRICS

Arena, J. M. (Editor): *Davidson's Compleat Pediatrician.* 9th ed. Philadelphia, Lea & Febiger, 1969, $19.50.

Barness, L. A., *et al.: Manual of Pediatric Physical Diagnosis.* 3d ed. Chicago, Year Book, 1966. Paper, $6.00.

Barnett, H. L.: *Pediatrics.* 14th ed. New York, Appleton, 1968. $24.50.

Cooke, R. E. and Levin, S. (Editors): *The Biologic*

Basis of Pediatric Practice. New York, Mc-Graw-Hill, 1968. $24.50.

Craig, W. S., *et al.: Care of the Newly Born Infant*. 4th ed. Baltimore, Williams & Wilkins, 1969. $15.75.

Gellis, S. S., and Kagan, B. M.: *Current Pediatric Therapy 5*. Philadelphia, Saunders, 1971. $25.00.

Green, M., and Haggerty, R. J.: *Ambulatory Pediatrics*. Philadelphia, Saunders, 1968. $22.50.

Hughes, J. G.: *Synopsis of Pediatrics*. 3d ed. St. Louis, Mosby, 1971. $14.50.

Keith, J. D.: *Heart Disease in Infancy and Childhood*. 2d ed. New York, Macmillan, 1967. $35.00.

Kempe, C. H., *et al.* (Editors): *Current Pediatric Diagnosis and Treatment*. Los Altos, Lange, 1970. $11.00.

Krugman, S., and Ward, R.: *Infectious Diseases of Children*. 4th ed. St. Louis, Mosby, 1968. $18.75.

Nelson, W. E., *et al.: Textbook of Pediatrics*. 9th ed. Philadelphia, Saunders, 1969. $21.50.

Schaffer, A. J., and Avery, M. E.: *Diseases of the Newborn*. 3d ed. Philadelphia, Saunders, 1971. $27.50.

Shirkey, H. C. (Editor): *Pediatric Therapy*. 4th ed. St. Louis, Mosby, 1971. $25.00.

Silver, H. K.: *Handbook of Pediatrics*. 9th ed. Los Altos, Lange, 1971. $6.50.

Comment: Barnett and Nelson are the standard comprehensive references. The book edited by Arena is shorter and cheaper. It is also good.

PERIPHERAL VASCULAR DISEASES (See cardiovascular diseases)

PHARMACOLOGY AND THERAPEUTICS

American Medical Association Council on Drugs: *A.M.A. Drug Evaluations*. Chicago, American Medical Association, 1971. $15.00.

Chatton, M. J., *et al: Handbook of Medical Treatment*. 12th ed. Los Altos, Lange, 1970. $6.50.

Conn, H. F. (Editor): *Current Therapy 1972*. Philadelphia, Saunders, 1972. $16.50.

DiPalma, J. R. (Editor): *Drill's Pharmacology in Medicine*. 4th ed. New York, McGraw-Hill, 1971. $24.50.

Dreisbach, R. H.: *Handbook of Poisoning: Diagnosis & Treatment*. 7th ed. Los Altos, Lange, 1971. $6.00.

Goodman, L. S., and Gilman, A.: *The Pharmacological Basis of Therapeutics*. 4th ed. New York, Macmillan, 1970. $25.00.

Melmon, K. L., and Morrelli, H. F. (Editors): *Clinical Pharmacology*. New York, Macmillan, 1971. paper $11.95; cloth $16.00.

Modell, W. (Editor): *Drugs of Choice 1972-1973*. St. Louis, Mosby, 1972. $21.50.

Physicians Desk Reference to Pharmaceutical Specialties and Biologicals. 26th ed. Annual. Oradell, New Jersey, Medical Economics, 1972. $11.00.

Washington University Department of Medicine. Rosenfeld, G. (Editor): *Manual of Medical Therapeutics*. 20th ed. Boston, Little, Brown, 1971. Paper, $7.50.

Comment: Of the general reference books in pharmacology, we have preferred DiPalma and the book of Goodman and Gilman. However, some of the other general textbooks are also good. The little manual on medical therapeutics written by Rosenfeld and his associates has been easy to use, popular, and cheap. New editions of this are frequent. The new book on clinical pharmacology of Melmon and Morrelli is good. One of the most useful sources of information on drugs is the new publication called "AMA Drug Evaluations."

PHYSICAL DIAGNOSIS (See diagnosis)

PHYSICAL MEDICINE AND REHABILITATION

Krusen, F. H. (Editor): *Handbook of Physical Medicine and Rehabilitation*. 2d ed. Philadelphia, Saunders, 1971. $25.00.

Licht, S.: *Rehabilitation and Medicine*. New Haven, Licht, 1968. $18.00.

Rusk, H. A.: *Rehabilitation Medicine: a Textbook on Physical Medicine and Rehabilitation*. 3d ed. St. Louis, Mosby, 1971. $19.90.

Comment: The books of Krusen and of Rusk are the standard references in the field.

POISONING (See pharmacology and therapeutics)

PREVENTIVE MEDICINE AND PUBLIC HEALTH

Clark, D. W., and MacMahon, B. (Editors): *Preventive Medicine*. Boston, Little, Brown, 1967. Paper, $11.50. Cloth, $16.50.

Hobson, W. (Editor): *The Theory and Practice of Public Health*. 3d ed. New York, Oxford University Press, 1969. $27.50.

Kilbourne, E. A., and Smillie, W. G. (Editors): *Human Ecology and Public Health*. 4th ed. New York, Macmillan, 1969. $11.95.

Sartwell, P. (Editor): *Roseneau's Preventive Medicine and Public Health*. 10th ed. New York, Appleton, 1972. $24.50.

Comment: If it were necessary to choose a single volume, we would prefer the book edited by Sartwell. It is quite recent (1972).

PSYCHIATRY

Detre, T. P., and Jarecki, H. G.: *Modern Psychiatric Treatment*. Philadelphia, Lippincott, 1971. $25.00.

Freedman, A. M., and Kaplan, H. I. (Editors): *Comprehensive Textbook of Psychiatry*. Baltimore, Williams & Wilkins, 1967. $24.75.

Hofling, C. K.: *Textbook of Psychiatry for Medical Practice*. 2d ed. Philadelphia, Lippincott, 1968. $10.00.

Kolb, L. C. (Editor): *Noyes' Modern Clinical Psychiatry*. 7th ed. Philadelphia, Saunders, 1968. $11.00.

Ulett, G. A., and Goodrich, D. W.: *A Synopsis of Contemporary Psychiatry*. 4th ed. St. Louis, Mosby, 1969. $10.50.

Comment: We have no special preference among these volumes.

PUBLIC HEALTH (See preventive medicine and public health)

PULMONARY DISEASES (including thoracic surgery)

Bates, D. V., *et al.: Respiratory Function in Disease: an Introduction to the Integrated Study of the Lung*. 2d ed. Philadelphia, Saunders, 1971. $24.00.

Baum, C. L. (Editor): *A Textbook of Pulmonary Disease*. 2d ed. Boston, Little, Brown, 1972. In preparation.

Crofton, J., and Douglas, A.: *Respiratory Diseases*. Philadelphia, Davis, 1969. $27.50.

d'Abreu, A. L., *et al: A Practice of Thoracic Surgery*. 3d ed. Baltimore, Williams & Wilkins, 1971. $41.50.

Fraser, R. G., and Pare, J. P.: *Diagnosis of Diseases*

of the Chest. Philadelphia, Saunders, 1970. 2 vols. $48.00.

Gibbon, J. H., *et al.: Surgery of the Chest.* 2d ed. Philadelphia, Saunders, 1969. $32.50.

Hinshaw, H. C., and Garland, L. H.: *Diseases of the Chest.* 3d ed. Philadelphia, Saunders, 1969. $25.00.

Lindskog, G. E.: *Thoracic and Cardiovascular Surgery with Related Pathology.* 3d ed. New York, Appleton, 1972. In Preparation.

Comment: The books of Baum and of Hinshaw are both good general texts in this field. The book of Baum is, at present, slightly more recent. We have no special preference among the three good thoracic surgery books which are listed.

RADIOLOGY AND NUCLEAR MEDICINE

Blahd, W. H. (Editor): *Nuclear Medicine.* 2d ed. New York, McGraw-Hill, 1971. $33.50.

Maynard, C. D.: *Clinical Nuclear Medicine.* Philadelphia, Lea & Febiger, 1969. $12.50.

Meschan, I.: *Roentgen Signs in Clinical Practice.* Philadelphia, Saunders, 1966. 2 vols. $38.00.

Moss, W. T., and Brand, W. N.: *Therapeutic Radiology; Rationale, Technique, Results.* 3d ed. St. Louis, Mosby, 1969. $24.50.

Paul, L. W., and Juhl, J. H.: *Essentials of Roentgen Interpretation.* 2d ed. New York, Harper & Row, 1965. $30.00. (A new edition is in preparation.)

Powsner, E. R., and Raeside, D. E.: *Diagnostic Nuclear Medicine.* New York, Grune & Stratton, 1971. $30.00.

Simon, G.: *Principles of Chest X-Ray Diagnosis.* 3d ed. New York, Appleton, 1971. $23.50.

Wagner, H. N.: *Principles of Nuclear Medicine.* 2d ed. Philadelphia, Saunders, 1972. In Preparation.

Comment: We have no strong preference among these books which relate to diagnosis. Moss is probably the best book on therapeutic radiology. The four books listed on nuclear medicine are all good. The books of Powsner and of Blahd both have the advantage of being quite recent (1971).

RENAL DISEASES (See kidney disease)

RHEUMATOLOGY (See arthritis and rheumatism)

SKIN (See dermatology)

SURGERY, GENERAL

American College of Surgeons. Committee on Pre and Post Operative Care: *Manual of Preoperative and Postoperative Care.* 2d ed. Philadelphia, Saunders, 1972. $8.50.

American College of Surgeons. Committee on Trauma: *Early Care of the Injured Patient.* Philadelphia, Saunders, 1972. In Preparation.

Anson, B. J., and McVay, C. B.: *Surgical Anatomy.* 5th ed. Philadelphia, Saunders, 1971. 2 vols. $45.00.

Ballinger, W. F., *et al.* (Editors): *The Management of Trauma.* Philadelphia, Saunders, 1968. $25.00.

Boyes, J. H. (Editor): *Bunnell's Surgery of the Hand.* 5th ed. Philadelphia, Lippincott, 1970. $34.00.

Didio, L. J. A.: *Synopsis of Anatomy.* St. Louis, Mosby, 1970. $17.75.

Dunphy, J. E., and Botsford, T. W.: *Physical Examination of the Surgical Patient.* 3d ed. Philadelphia, Saunders, 1964. $8.50 (4th ed. in preparation; due 1973).

Ferguson, L. K.: *Surgery of the Ambulatory Patient.* 4th ed. Philadelphia, Lippincott, 1966. $17.00.

Goss, C. M. (Editor): *Gray's Anatomy of the Human Body.* 29th ed. Philadelphia, Lea & Febiger, 1972. In Preparation.

Hardy, J. D. (Editor): *Critical Surgical Illness.* Philadelphia, Saunders, 1971. $28.00.

Jones, P. (Editor): *Clinical Pediatric Surgery: Diagnosis and Management.* Philadelphia, Davis, 1970. $15.00.

Maingot, R.: *Abdominal Operations.* 5th ed. New York, Appleton, 1969. 2 vols. $45.50.

Mustard, W. T., *et al.: Pediatric Surgery.* 2d ed. Chicago, Year Book, 1969. 2 vols. $50.00.

Nealon, T. F., Jr.: *Fundamental Skills in Surgery.* 2d ed. Philadelphia, Saunders, 1971. $11.75.

Rhoads, J. E., *et al.* (Editors): *Surgery: Principles and Practice.* 4th ed. Philadelphia, Lippincott, 1970. $24.00.

Schwartz, S. I., *et al.* (Editors): *Principles of Surgery.* New York, McGraw-Hill, 1969. Vol. I, $24.50; Vol. II, $29.50.

Wilson, J. L. (Editor): *Handbook of Surgery.* 4th ed. Los Altos, Lange, 1969. $6.00.

Comment: Of the general texts in this field, our first choice is the book edited by Schwartz. The book edited by Rhoads is also good. We have no special preference among the anatomy books listed. Some other excellent volumes on surgical subjects are listed under other headings such as Pulmonary Disease (thoracic surgery), Orthopedics, Urology, etc.

THERAPEUTICS (See pharmacology and therapeutics)

TOXICOLOGY (See pharmacology and therapeutics)

UROLOGY (See also kidney disease)

Campbell, M. F., and Harrison, J. H. (Editors): *Urology.* 3d ed. Philadelphia, Saunders, 1970. 3 vols. $110.00.

Dodson, A. I.: *Urological Surgery.* 4th ed. St. Louis, Mosby, 1970. $35.00.

Emmett, J. L., and Whitten, D. M.: *Clinical Urography: An Atlas and Textbook of Roentgenologic Diagnosis.* 3d ed. Philadelphia, Saunders, 1971. 3 vols. $84.00.

Flocks, R. H., and Culp, D.: *Surgical Urology* (Handbook of Operative Surgery Ser.). 3d ed. Chicago, Year Book, 1967. $13.50.

Glenn, J. F., and Boyce, W. H. (Editors): *Urologic Surgery.* New York, Harper & Row, 1969. $35.00.

Smith, Donald R.: *General Urology.* 6th ed. Los Altos, Lange, 1969. $8.00.

Comment: For the urologist, the detailed information in the volumes edited by Campbell will be very useful. However, this is an expensive publication ($110.00). The smaller books listed are all good, and any of these would be a helpful source of information for a physician who is not a urologist. We do not usually list books as highly specialized as that of Emmett and Whitten, but both urologists and radiologists have recommended this book to us.

X-RAY (See radiology)

OTHER GENERAL REFERENCE VOLUMES

Blakiston's Gould Medical Dictionary. 3rd ed. New York, McGraw-Hill, 1972. $14.50.

Chatton, M. J., and Sanazaro, P. J. (Editors): *Current Medical References.* 6th ed. Los Altos, Lange, 1970. Paper, $12.00.

Cooper, P.: *Ward Procedures and Techniques.* New York, Appleton, 1967. Paper, $6.75.

Dorland's Illustrated Medical Dictionary. 24th ed. Philadelphia, Saunders, 1965. $13.50.

Fisher, J. C.: *Clinical Procedures: A Concise Guide for Students of Medicine.* Baltimore, Williams & Wilkins, 1970. Paper, $3.95.

Gordon, B. L. (Editor): *Current Medical Information and Terminology.* Chicago, American Medical Association, 1971. $8.00.

Grace, W. S., and Kennedy, R. S.: *Medical Resident's Manual.* 3d ed. New York, Appleton, 1971. Paper, $6.75.

Jablonski, S. R.: *Illustrated Dictionary of Eponymic Syndromes and Diseases.* Philadelphia, Saunders, 1969. $12.75.

Krupp, M. A., *et al.: Physician's Handbook.* 16th ed. Los Altos, Lange, 1970. $6.00.

List of journals available in nearest back-up medical library.

Magalini, S.: *Dictionary of Medical Syndromes.* Philadelphia, Lippincott, 1971. $18.00.

Merck, Sharp, & Dohme Research Laboratories: *The Merck Manual of Diagnosis and Therapy.* 12th ed. Rahway, New Jersey, Merck, 1971. $8.50.

National Library of Medicine: *Abridged Index Medicus* (monthly and annual cumulation). Washington, Government Printing Office. Monthly, $12 per year; cumulation, $10.00.

National Library of Medicine: *Index Medicus* (monthly and annual cumulation). Washington, Government Printing Office. Monthly, $63 per year; cumulation $84.00.

Stedman's Medical Dictionary. 22nd ed. Baltimore, Williams & Wilkins, 1972. $18.50.

Comment: The book edited by Chatton and Sanazaro can be very helpful in clinical practice. They have reviewed world literature in order to select the journal articles which have greatest relevance to clinical practice. These articles have been very well indexed so that one can identify quickly a few well selected references on almost any clinical subject. The three dictionaries listed are comparable. The *Abridged Index Medicus* has considerable potential for serving clinical practice. It indexes the literature published in 100 of the principal English language journals. A substantial majority of the literature of clinical relevance is indexed in this new publication which costs only $10.00 per year for the cumulated index. For the small hospital or doctor's office, the monthly issues alone of the *Index Medicus* or *Abridged Index Medicus* have limited utility. On the other hand, together with the *Cumulated Index* and the *Cumulated Abridged Index* have considerable clinical potential if used appropriately. □

I NEED YOUR HELP!

The important activities of your association are carried out through appointed councils and committees—all members of the OSMA are encouraged to contribute to the organization by volunteering for service during the 1972-73 fiscal year. Indicate your interest by checking one or more of the following areas of interest, sign and mail to: President S. R. McCampbell, MD, OSMA, 601 NW Expressway, Oklahoma City, Oklahoma 73118.

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News From The Oklahoma State Department of Health

TURTLE-ASSOCIATED SALMONELLOSIS

Pet turtles are of documented potential in the transmission of salmonellosis to humans. No less than a score of papers in the recent scientific literature have noted an association between pet turtles and salmonella gastroeinteritis.

The studies of Williams, *et al.* (JAMA, May 3, 1965) showed 16 serotypes of salmonella as being turtle associated. Follow-up of these serotypes demonstrated, in addition to the original case, five index cases where turtles were the source of the infection. Similar findings have been made by Kaufman, *et al.* (Public Health Reports, September 1967) and Baker, *et al.* (Archives of Environmental Health, January 1972). Work by others, including specialists from the National Center for Disease Control, have demonstrated salmonellae not only in the turtles themselves, but in pet turtle food, specifically manufactured for the turtles.

Transmission generally occurs where turtles and small children are present in the same home. Contamination of the hands during play and caring for the animals is the most common occurrence. Changing of turtle water in the kitchen sink is another potential mechanism for transmission.

Although the salmonellae have been associated with some species of turtles for years, it was only fairly recently that the more common pet turtles were found carrying the organism. Secondly, fewer than 1% of salmonella infections were formerly thought to be associated with turtles. Clearly, Lamm's work in Connecticut (Center for Disease Control, USPHS) showing that up to 27% of human infections were associated with pet turtles, was cause for concern.

Several states have enacted legislative controls over the distribution and sale of pet turtles. The federal government recently enacted regulation of shipment and sales of turtles. The State of Oklahoma will deal with the problem during the interim session of the State legislature with a regulation concerning several kinds of exotic and dangerous pets. □

COMMUNICABLE DISEASES IN OKLAHOMA FOR MARCH, 1972

Disease	March, 1972	March, 1971	Feb., 1972	Total to Date 1972	Total to Date 1971
Amebiasis	4	4	3	8	17
Brucellosis	—	—	—	—	—
Chickenpox	12	27	39	88	70
Encephalitis, infect.	—	3	2	2	7
Gonorrhea	692	587	856	2307	1762
Hepatitis, infect. & serum	54	70	66	160	175
Leptospirosis	—	—	—	—	—
Malaria	1	14	—	1	33
Meningococcal infections	2	2	1	3	5
Meningitis, aseptic	2	3	3	6	39
Mumps	18	63	40	89	117
Rabies in animals	41	63	14	63	118
Rheumatic fever	—	1	9	10	5
Rocky Mt. spotted fever	—	—	—	1	1
Rubella	—	9	—	2	32
Rubella, congenital syn.	—	—	—	—	—
Rubeola	—	193	—	1	551
Salmonellosis	9	6	7	19	40
Shigellosis	9	3	4	14	27
Syphilis	66	118	126	272	336
Tetanus	—	—	—	—	—
Tuberculosis, new active	7	3	17	40	44
Tularemia	1	—	—	1	—
Typhoid fever	—	—	—	—	—
Whooping cough	1	2	3	5	6

OSMA's 66th Meeting Now History

Oklahoma physicians closed their 66th annual meeting with a banquet on Saturday evening, May 20th. Nearly 1,000 persons had attended the three-day meeting in Oklahoma City's Skirvin Hotel.

During the Saturday night banquet, Stanley R. McCampbell, MD, Oklahoma City, assumed the Presidency of the 2,300 member association when Lucien M. Pascucci, MD, Tulsa, stepped down.

Annual elections for the OSMA were held during the closing session of the OSMA House of Delegates Thursday evening, May 18th. C. Riley Strong, MD, El Reno, was elected to serve one year as President-Elect of the OSMA and then will assume the presidency at the association's next annual meeting in April, 1973.

In other elections, Robert J. Hogue, Jr., MD, was re-elected to the vice-presidency for another year. Other officers that were re-elected included Roger Reid, MD, of Ardmore, and Samuel N. Stone, MD, of Oklahoma City, as Speaker and Vice-Speaker of the OSMA House of Delegates.

Scott Hendren, MD, Oklahoma City, and Harlan Thomas, MD, Tulsa, were re-elected to two-year terms by the House of Delegates as delegates to the American Medical Association. Their alternates will be Rex Kenyon, MD, Oklahoma City, and Orange Welborn, MD, Ada.

The annual meeting of the association's Board of Trustees was held Wednesday night, May 17th. At that time, C. Riley Strong, MD, stepped down as chairman of the Board and M. Joe Crosthwait, MD, Midwest City was elected to succeed him. Jerald Kethley, MD, Shawnee, was elected vice-chairman of the Board to replace Orange Welborn, MD.

The House of Delegates was also called upon to conduct election for several seats on the OSMA Board of Trustees. Thomas Rhea, MD, Idabel, and Bill Woodruff, MD, Hugo, were re-elected as the Trustee and Alternate Trustee for District XI of the OSMA. Frank Clark, MD, Ardmore, was elected Trustee from District XII to replace Orange M. Welborn, MD, Ada, who was ineligible for re-election. Clark's alternate will be Clarence Taylor, MD, Ada. William R. Cheatwood, MD, was ineligible for re-election as Trustee of District XIII and was replaced by Paul Vann, MD, Lawton. His alternate will be A. Craig Roberson, MD, Anadarko.

Fred Sellers, MD, Mangum, moved up from Alternate to Trustee for District XIV to replace Charles L. Tefertiller, MD, Altus. His alternate will be Lowell N. Templer, MD, Altus.

During their one-day deliberations, members of the House of Delegates considered 13 reports from OSMA's Councils and Committees, the Report of the President, Report of the Board of Trustees, the Treasurer's Report, and 17 Resolutions introduced by county medical societies and individual association members.

A complete report of all actions taken by the House of Delegates will be published in the next issue of the *OSMA Journal*.

Following is a brief description of a few of the highlights of the Delegates actions.

- The OSMA President was author-



Some of the newly elected officers of the OSMA are (l to r) Roger Reid, MD, Ardmore, Speaker of the House of Delegates; Robert J. Hogue, MD, Guthrie, Vice-President; C. Riley Strong, MD, El Reno, President-Elect; Stanley R. McCampbell, MD, Oklahoma City, President; M. Joe Crosthwait, MD, Midwest City, Chairman of the Board of Trustees. Standing (l to r) Clarence P. Taylor, MD, Ada, Alternate Trustee District XII; S. N. Stone, MD, Oklahoma City, Vice-Speaker of the House of Delegates; Harlan Thomas, MD, Tulsa, Delegate to the AMA; Thomas E. Rhea, MD, Idabel, Trustee, District XI; Orange M. Welborn, MD, Ada, Alternate Delegate to the AMA; and, Scott Hendren, MD, Oklahoma City, Delegate to the AMA. Other officers who were elected are Rex Kenyon, MD, Oklahoma City, Alternate Delegate to the AMA; Bill E. Woodruff, MD, Hugo, Trustee, District XI; Frank W. Clark, MD, Ardmore, Trustee, District XII; Paul N. Vann, MD, Lawton, Trustee, District XIII; A. C. Roberson, MD, Anadarko, Alternate Trustee, District XIII; Fred W. Sellers, MD, Mangum, Trustee, District XIV and Lowell N. Templer, MD, Alternate Trustee, District XIV. □

ized to immediately issue a memorandum to the entire membership in support of a branch school of the University of Oklahoma School of Medicine in the Tulsa area as opposed to a College of Osteopathy.

● Due to increased costs in publishing the *OSMA Journal* and continuing loss of revenues from exhibits at the OSMA Annual Meeting, the House adopted a recommendation that it contemplate a dues increase for 1973.

● The House again voted to retain mandatory AMA dues as a prerequisite to membership in the OSMA.

● A resolution was adopted urging the O. U. Board of Regents, the Board of Regents for Higher Education, the Governor of the State, and the Senate and the House of Representatives to guarantee the adequate financial support of the Oklahoma Health Sciences Center "in order that the expectations of the people of Oklahoma for the highest quality of health care be thereby assured."

● The Council on Professional Education was instructed to attempt to utilize the Televised Instruction System for continuing education and asked to work out details with the medical school permitting practice physicians to take clinical elective courses.

● The OSMA Legislative Committee was authorized to invite special guests, county society officials and others to participate in deliberations of the committee when it is studying legislation pending before the Oklahome Senate and House of Representatives.

● The Board of Trustees is to develop a survey form to be submitted to the association members inquiring of their attitude on abortions. The survey is to include a question regarding the specialty practiced by the respondant and his opinion as to whether or not the OSMA should take a position on the abortion question. The results of the survey will be furnished to OSMA members, the legislature, and the public. In addition, members will be surveyed as to their opinion on the delivery of contraceptive services to sexually active teenagers without parents consent.

● The name of the OSMA Medical Insurance Review Committee was changed to the more appropriate "Peer Review Cimmittee" of the OSMA.

● A new "Medical-Legal Interprofessional Code" of cooperation between physicians and attorneys was adopted by the House. The code was adopted last December by the Oklahoma Bar Association. It will be printed in pamphlet form and distributed to all members of the Association.

● It was recommended that the OU College of Medicine be asked to officially change their bylaws to provide at least 50% of the appointments to the admissions board be composed of primary care physicians in private practice.

● A recommendation was adopted by the House urging the Medical School administration to dedicate the two-year medical school in Tulsa to the clinical training of primary care physicians and "further, that they actively seek new and innovative techniques to accelerate and expand such training."

● The medical school was also urged to "re-evaluate, and if necessary reorganize, its Family Practice Residency Program to make it more responsive to the needs of Oklahoma communities."

● A resolution was adopted stating, "be it resolved that the Oklahoma State Medical Association reaffirm its previous policy of urging all physicians in Oklahoma to refuse assignment from third party payors, and to negotiate, direct, personal, contracts with patients that will properly serve their medical needs, and be it further resolved, that the OSMA will give moral support and encouragement to those of its members who might be harassed as a result of refusing assignment."

● Governor David Hall was "commended and supported for his declaration of intent to maintain Children's Memorial Hospital inpatient services and maintain emergency room services at the Health Sciences Center. . ." The resolution went on to urge the legislature and the citizens of Oklahoma to "join" the Oklahoma State Medical Association in support of the Health Sciences Center in this crisis in order to maintain the high quality of medical education and medical care that has been carried out in the past."

● An increase in the professional liability rates for the OSMA's endorsed program was announced. The Insurance Company of North America, through its subsidiary, the Pacific Employers Indemnity Company, asked for a 30% increase but compromised for a 21.7% overall in-



Eleven OSMA Past-Presidents attended a breakfast in their honor on Friday, May 19th. Present were (seated, l to r) R. Q. Goodwin, MD, Oklahoma City; Joe L. Duer, MD, Woodward; Harlan Thomas, MD, Tulsa; George H. Garrison, MD, Oklahoma City. Standing (l to r) Clinton Gallaher, MD, Shawnee; Hillard E. Denyer, MD, Bartlesville; H. K. Speed, MD, Sayre; Ed Calhoon, MD, Beaver; John Flack Burton, MD, Oklahoma City; Scott Hendren, MD, Oklahoma City; and, Lucien Pascucci, MD, Tulsa. □

crease. Even with this rate increase, Oklahoma physicians will still be paying only about 50% of the manual rates for professional liability in most classifications. A comparison with surrounding states and other representative states throughout the nation show that Oklahoma's Professional Liability picture is about the best.

● The Alcoholism and Drug Abuse Committee of the medical association was instructed to update its "Drug Abuse Treatment Manual" for republication, and to consider publishing a directory of all drug abuse informational programs throughout the state in an attempt to help coordinate them.

● A statewide "polio Sunday" campaign was approved by the House to be set for September 10th. The purpose will be to bring Oklahoma's polio immunization level up. A recent study of pre-school children indicates that almost one-third of that age group did not have adequate polio immunity. □

Allergists To Meet In Seattle

The American Association for Clinical Immunology and Allergy will sponsor an intensive instructional course in current concepts in allergy and clinical immunology on July 17th, 18th and 19th. Seattle, Washington, will be host city for the three-day meeting.

The course is being designed to assist physicians in their preparation for the forthcoming certification examination to be given by the new Conjoint Board in Allergy. At the conclusion of the course, each participant will be provided with question forms for a self-assessment examination and a complete course outline with synopsis of lectures.

Additional information on the course may be obtained from the American Association for Clinical Immunology and Allergy, P.O. Box 912 DTS, Omaha, Nebraska 68101. □

Meet the President-Elect

On Thursday evening, May 18th, the OSMA House of Delegates elected C. Riley Strong, MD, as President-Elect of the 2,300 member organization. He will serve in that capacity for one year and then will take over as President during the association's 1973 meeting in Tulsa.

Doctor Strong has been in the private practice of medicine in El Reno, Oklahoma, since 1946. He graduated from Oklahoma University College of Medicine in 1943 and took a rotating internship at the US Naval Hospital, Longbeach, California.

During World War II he served 36 months in the United States Navy as a medical officer. Of this time 14 months were spent as a ship's physician and ten months overseas.

He was born on February 3rd, 1920, in Nashville, Kansas, and took his premedical education at Oklahoma A & M College, Stillwater.

He and his wife, Ruth Ellen, have three children: Clinton, age 25; Stephen, age 22; and Sharon, age 20. Clinton has just completed his MD degree and is currently in his residency training in California, while Stephen is studying pharmacology at Weatherford.

Doctor Strong has served as a member of the OSMA Board of Trustees and has been chairman of the Board for the past four years. He has also been active in the American Academy of Family Physicians and has served that organization as its state president in 1965, and as a delegate to the congress of the AAFP, where he is presently a member of the Membership and Credentials Committee. Doctor Strong was one of the charter members of the Oklahoma chapter of the academy. □



C. RILEY STRONG, MD

Course in Psychiatry Offered Physicians

The Department of Psychiatry and Behavioral Sciences and the Office of Continuing Medical Education for Physicians, University of Oklahoma Health Sciences Center, is now accepting applications for the 1972-73 Course in Psychiatry for Physicians. This course is accredited by the American Academy of General Practice and any qualified physician in Oklahoma is eligible to apply. The class will meet each Wednesday from 1:30 to 5:00 p.m., September 13th, 1972 through May 16th, 1973. Deadlines for submitting applications is July 1st, 1972. For further information, contact Boyd K. Lester, MD, P.O. Box 26901, Oklahoma City 73190, telephone 405 235-9434. □

Physician Seeks Information on Biting Insects

Claude A. Frazier, MD, is compiling case reports of allergic reactions to biting insects, *i.e.* mosquitos, fleas, kissing bugs, bed bugs, gnats and flies, including horsefly, sandfly, deerfly. He is also interested in reactions to fire ants. He would appreciate hearing from physicians who will supply him with case reports including the history of the type of reaction and complications, if any; the immediate treatment; and, results from desensitization.

Physicians interested in helping with this study may mail their reports or summaries to Doctor Frazier, 4-C Doctors Park, Asheville, North Carolina 28801. □

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Oklahoma City's proposed Mercy Health Center.

Health Center Construction Slated

Construction of Oklahoma's first hospital to have all private rooms will get underway in June.

Designed by Benham-Blair and Affiliates, Oklahoma City, national architects-engineers-consulants, the new seven-story Health Center in northwest Oklahoma City will incorporate facilities designed to provide the maximum patient comfort and convenience at the most economical operating cost.

Mercy will have 400 rooms. The private room concept is being used to provide the most effective care available. It will offer added privacy and will enable it to be used as an examining room, thus relieving the patient of the need to be moved.

A nurse's alcove for each room has been designed to enable the staff to offer better care. It will include a "Nurserver," which is a cabinet with doors inside the nurse's alcove portion of the patient's room and on the outside into the corridor. This will contain the patient's supplies, equipment, medication and chart, which will enable the doctors and nurses to give special attention and better personal care to each individual.

A comprehensive communication system will also be used in the health center. It will contain an Administrative Control Center that will serve as a central communications system. The ACC will enable nurses to more quickly serve a patient's needs, because when a nurse is needed, all the ACC needs to do is press a button and through a pocket pager weighing only 4 ounces, she will receive a buzz tone and a one-way message.

The Benham-Blair design also provides for a closed circuit television to be used extensively for education and medical use.

The closed circuit system can be used as an orientation and to better inform patients of how they can make themselves more comfortable, healthier and other ways of aiding themselves. They will also be able to view Sunday church services from the hospital chapel on the television and it will be possible to televise educational demonstrations such as showing new mothers how to care for newborn babies.

The new Mercy Health Center will also be the first in the State of Oklahoma to use an overhead two-way monorail system for cart transportation.

The overhead monorail has been designed so that it will not be noticeable in hallways. They will be loaded at a central location, and will be delivered to upper floors through elevator type equipment. They can be removed from the elevator and used on each floor. This system will provide a quick and efficient delivery of supplies and discarded items can be returned without constantly having carts in the hall taking up vital space.

The new Mercy Health Center will use a rather unusual arrangement in the surgical and obstetrical suites. These areas will be side-by-side, which will eliminate duplication of certain operating equipment and personnel and can be used in both areas. Also, in the event of an extreme emergency situation, both areas could be used for whatever is most needed at the time.

Bids for the $25.5 million dollar project were received from seven companies on May 10th.

The contract for the project was expected to be awarded in late May, with construction to begin in June.

Occupancy of the 400-bed center is scheduled for the Fall of 1974. □

Average Hourly Earnings of Physicians Computed

Based on an average workweek of 60 hours, the average hourly earnings of a physician in 1971, were $12.92. This information was computed by the medical socioeconomic department of the Michigan State Medical Society.

At the same time the MSMS reported the above, it also reported that an electrician in the Detroit area, if he worked 60 hours a week, would earn $44,179 a year. □



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House Passes Minimum Wage For Hospitals And Nursing Homes

The U. S. House of Representatives finally ended two days of debate and took action on a new minimum wage bill for hospitals and nursing homes. A move was made to increase minimum wage in one fell swoop from $1.60 to $2.00 an hour. This was finally defeated in a compromise amendment.

Hospitals and Nursing Homes were first brought under the minimum wage law in 1966. The new law will raise the minimum wage to $1.70 an hour 60 days after its final enactment. It would then hit $1.80 an hour one year later and the $2.00 mark on January 1st, 1974.

In the meantime the Senate Labor and Public Welfare Committee is still working on its own version of the minimum wage amendments. Until one or the other of the two bills makes it all the way through the legislative process, the minimum wage will remain the same.

A strong push was put on by the American Nursing Home Association to freeze nursing home salaries at $1.60 an hour. The move was narrowly defeated by a vote of 55 to 52.

The House passed bill does not change overtime exceptions for hospitals and nursing homes, but it is expected that the Senate bill will eliminate the exceptions. □

Dennis Portrait Presented To Center



Participants in ceremonies unveiling a portrait of James L. Dennis, MD, former dean of the University of Oklahoma College of Medicine and executive vice-president of the Health Sciences Center, include, at left, Robert M. Bird, MD, who succeeded him as dean, and Robert E. Engles, MD, Durant, College of Medicine Alumni Association president, and, right, Elmer Ridgeway, MD, Oklahoma City, alumni past-president. Alumni commissioned the portrait, painted by Oklahoma City artist Dick Goetz, for presentation to the Health Sciences Center. Doctor Dennis left in 1970 to become University of Arkansas vice-president for health sciences. He and Mrs. Dennis were honored at the unveiling luncheon May 11th at the Faculty House. □

Doctors-Lawyers To Meet at Arrowhead

A two-day Medical-Legal Institute of interest to all Oklahoma physicians and attorneys is being jointly sponsored by the OSMA and the Oklahoma Bar Association at Oklahoma's beautiful Arrowhead Lodge on Lake Eufaula, July 21st and 22nd.

Jointly planned by both professionals, the two-day meeting will cover such topics as professional corporations, workmen's compensation, the new medical examiners law, privileged communications, and malpractice arbitration.

In addition to the educational portions of the program, the social aspects will also be stressed. A cocktail party is scheduled for early Friday evening, and cocktails and a buffet dinner on Saturday evening. A registration fee of $35 per person is being charged to cover the cost of course materials and the social functions. However, it will be necessary to purchase tickets to the Saturday evening buffet for wives or other guests for only $4.00.

The Friday evening cocktail party is being scheduled early so that persons attending the institute will have time to go to Krebs, Oklahoma, for dining in one of that communities' outstanding Italian Restaurants . . . Pete's Place, the Isle of Capri, or Giacomos.

The following is a brief listing of the topics to be given on the two days:

Friday — professional corporations, new interprofessional code, workmen's compensation, uniform consumer credit code, and a demonstration on an examination and cross-examination of a physician witness.

Of specific interest to attorneys will be talks on the limitations of X-ray, EEG, and an orthopedic examination demonstration.

The new medical examiner's law will be first thing on the program Saturday morning. A discussion of the disease reporting now required for driver's licence revocation, and a section of privileged communications will also be held.

The final discussion for Saturday afternoon will be on the subject of malpractice arbitration.

Physicians wishing to attend the two-day meeting should contact the Oklahoma State Medical Association.

Special emphasis is being placed on the uniform consumer code. This law directly effects both professions economically. In addition, attorneys know the proper advise to be given to their physician-clients.

Physicians will be particularly interested in the Saturday presentation by Leroy Carpenter, MD, Oklahoma's Commissioner of Health. He will be speaking on disease reporting as it relates to the revocation of a driver's license. □

Commercial Health Insurors Take Lumps

Investigations into the workings of the commercial health insurance industry are being conducted by Senator Phillip A. Harts, Senate Anti-trust and Monopoly Sub-Committee.

First to come under fire was the "Medical Insurance Bureau of Greenwich, Connecticut" which maintains a computerized data bank of medical information on nearly 12 million persons. Executive Director of MIB revealed that it had 700 member companies, all of whom write life insurance and used the service to warn them about bad health risks among applicants.

Members of the Senate Anti-trust Sub-Committee charge that MIB information is also being used to deny issuance of individual health policies to persons who may be a bad risk. Questioning of several witnesses revolved around the same theme that commercial health insurors are skimming off the cream of the crop in group policies by attempting to screen out people with health problems who are in the most need of health insurance.

United Auto Workers President Leonard Woodcock charged, "the insurance companies want to sell sickness insurance to healthy people." He went on to say that commercial insurance companies have failed to monitor the appropriateness of medical bills they handle for Medicare and have a "dismal record of cost control." Woodcock advocated the end of the role of private carriers in Medicare and Medicaid, federal regulations for the industry, public accountability with restrictions on profits, standardized benefits packages, and an end to misleading advertising.

While pointing with pride to their many accomplishments representatives from the various insurance companies also admitted to some failings. Aetna Life and Casualty President Donald M. Johnson acknowledged that the health insurance industry can't handle high risk people and those with the incomes too low to pay premiums. He went on to suggest that perhaps the government should do the job.

Pennsylvania's controversial Insurance Commissioner, Doctor Herbert S. Denenberg, blasted the commercial carriers and said that the public would be far better served if Blue Cross and Blue Shield were given a monopoly. While stating that he doesn't believe in a total federal takeover of the health insurance system, he would prefer to see tough federal standards administered through the state. □

Actions By Other State Societies Noted

March, April and May are the busiest months for state medical societies throughout the nation. Like the OSMA, which has its annual meeting in May, most state societies choose this time of year to conduct their annual business meetings.

The Oregon Medical Association took three note worthy actions. In the first, the House of Delegates of Oregon directed that the Bylaws Committee prepare amendments to provide for the election of AMA delegates and alternates by statewide ballots among its members.

The Oregonians also favored the removal of marijuana from classification as a dangerous drug, and supported the position that possession for personal consumption should not be considered a felony. This latter was a position taken by the Oklahoma State Medical Association two years ago. In a related action, the House of Delegates called for adoption of the model state controlled substances act by the Oregon State Legislature.

The Idaho Medical Association rejected mandatory study requirements for continuing medical education. The House of Delegates directed a continuing study of methods of motivating members toward continuing education based on individual need.

Michigan doctors, during their Spring meeting, voted to express their support for a bill pending before their state legislature which would allow physicians to provide contraceptive assistance and counsel to teenagers without parental consent. They also adopted a resolution calling for MSMS to support legislation which would change the sex education laws of that state to allow the teaching of birth control. □

Drug Treatment Program Set For Little Rock VA

Veterans seeking voluntary treatment for drug abuse problems can now be referred to the VA Hospital in North Little Rock, Arkansas.

The basic treatment program is of three months duration, plus optional periods of additional time if the veteran desires to continue in treatment. Essentially the program is divided into four phases as follows: (1) first week's residence in the detoxification area, (2) second week in a candidacy evaluation status, and (3) if accepted, the patient is then placed in a treatment program for ten weeks, and (4) discharge and outpatient treatment unless the veteran and staff mutually agree to an extension of program time for special treatment or planning.

The program includes supervised detoxification, and special attention to personal living problems through the use of group psychotherapy.

Once the patient has entered the program, he may see no visitors for the first 37 days in the hospital and then he is allowed visitors only at specific visiting hours and under very strict rules.

For services in the drug treatment program, a veteran is defined as a man who has had a period of active duty in the military service, other than for training purposes and has a drug problem. Patients can be admitted at any time during the days of the week by seeing the physician in the admissions office during the hours of 8:30 a.m. and 4:00 p.m. He must bring with him proof of his military service. □

Current G.U. Research

Gantanol® in animals (sulfamethoxazole)



Control



12.5 mg sulfamethoxazole/kg of body weight



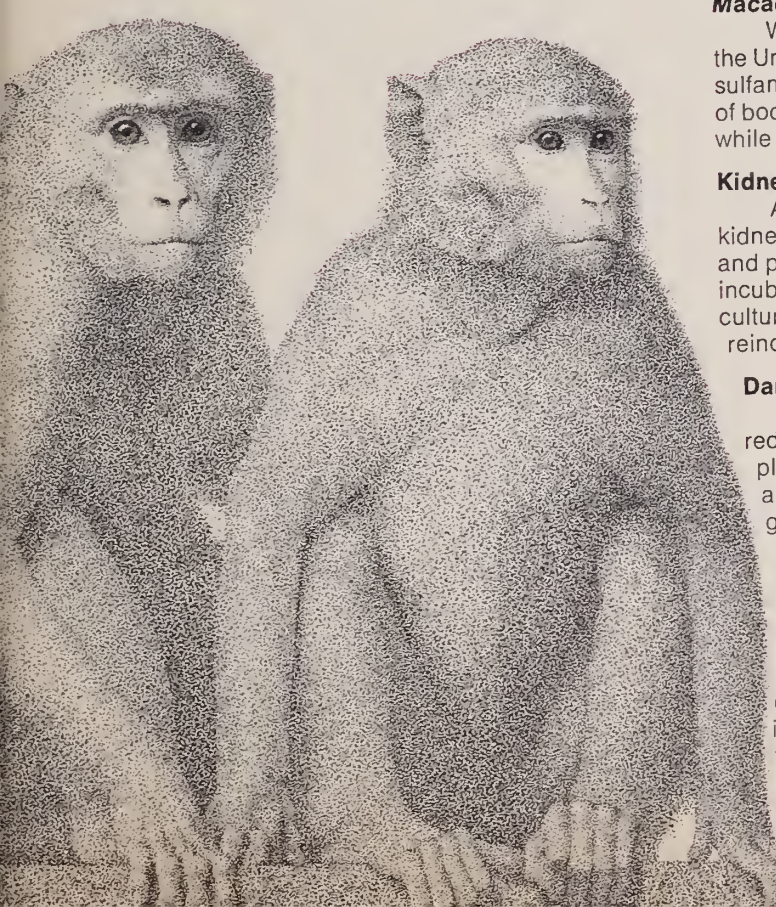
50 mg of sulfamethoxazole/kg of body weight



100 mg of sulfamethoxazole/kg of body weight

Tissue slice technique maps renal distribution in animal studies

Please note that while the method described may add to the knowledge of how antibacterial agents are distributed in the kidney of this animal, no conclusions can be drawn from this study relative to the drug's distribution, effect or use in humans, as it is not possible to extrapolate animal data to humans.



Gantanol® (sulfamethoxazole) administered to *Macaca speciosa* monkeys

Working with *Macaca speciosa* monkeys, researchers at the University of Arkansas Medical Center administered sulfamethoxazole at doses of 12.5 mg, 50 mg and 100 mg/kg of body weight. Each dosage level was given to three animals while three were left untreated as controls.*

Kidneys inoculated with *Staphylococcus aureus*

After 2½ hours, the 12 monkeys were sacrificed and their kidneys frozen with CO_2. Sagittal tissue slices were prepared and placed on blood agar bacteriological plates. They were incubated at 37°C. for 1½ hours. *Staphylococcus aureus* broth culture was then used to inoculate the tissue and slices were reincubated.*

Dark staining reveals heavy bacterial growth

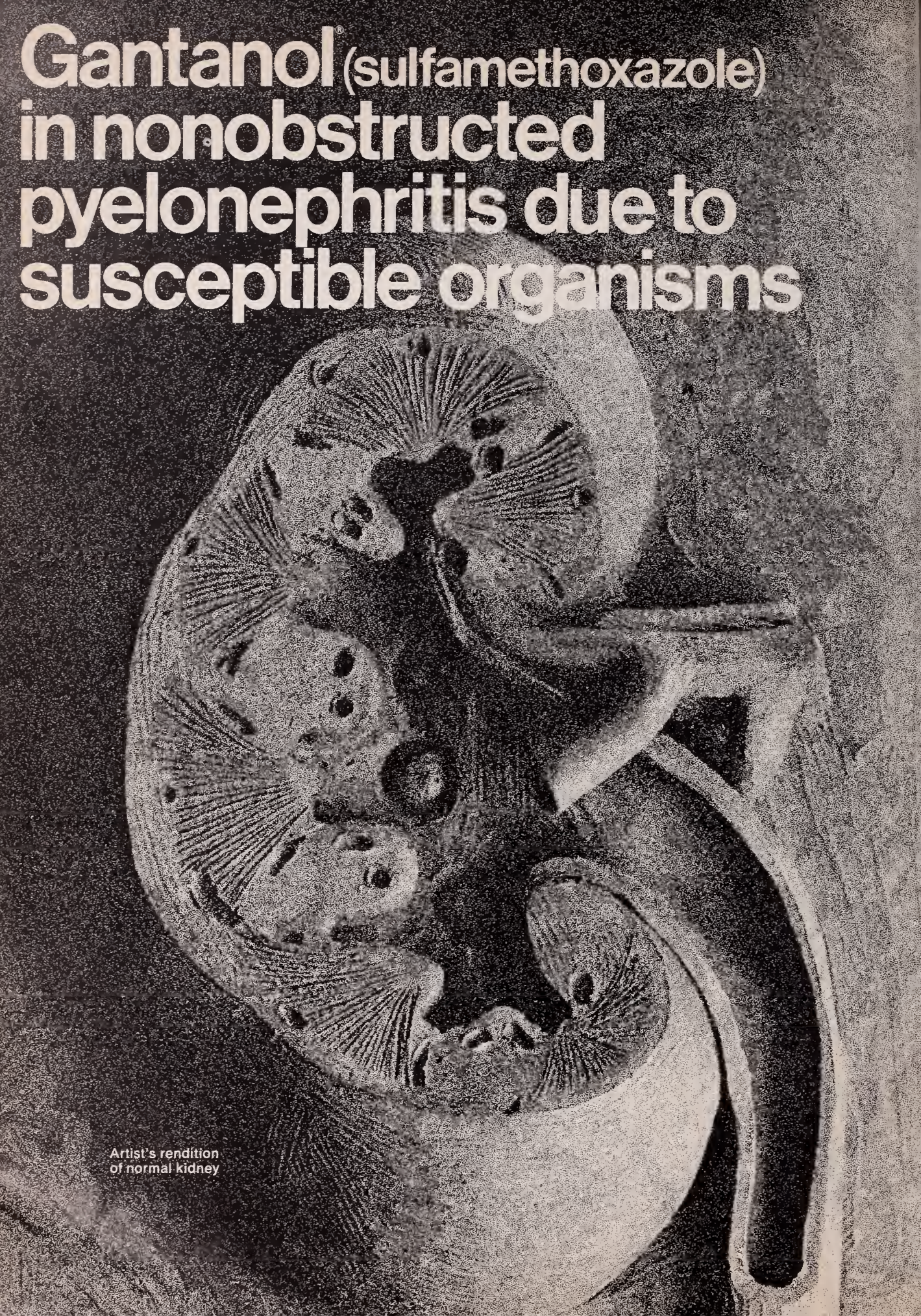
A solution of triphenyltetrazolium chloride, which turns a reddish purple in the presence of bacteria, was added to the plates after 6 hours. Renal slices from the untreated control animals consistently demonstrated heavy bacterial growth, as evidenced by dark staining.*

Distribution throughout *Macaca speciosa* renal parenchyma

At the dosage of 12.5 mg/kg of body weight, a diffuse stain pattern indicated partial inhibition of bacterial growth. Renal slices from monkeys given the 50 and 100 mg/kg doses showed no staining, indicating complete bacterial inhibition and *suggesting* antibacterial distribution throughout the parenchyma.*

*Mobley, J. E.; Redman, J. F., and Robbins, R. P.: *Surg. Gynec. Obstet.*, *131*:1122, 1970.

Gantanol® (sulfamethoxazole) in nonobstructed pyelonephritis due to susceptible organisms



Artist's rendition of normal kidney

Establishes antibacterial levels in blood and urine in from 2 to 3 hours

In from 2 to 3 hours of the initial 2-Gm adult dose, effective antibacterial levels of Gantanol® (sulfamethoxazole) are achieved in both blood and urine. This prompt, early treatment in acute nonobstructed pyelonephritis may help avert possible chronic sequelae.

Controls primary bacterial offenders

Antibacterial Gantanol (sulfamethoxazole) controls susceptible *E. coli*, the most common cause of urinary tract infections. It is also effective against other susceptible gram-negative and gram-positive urinary pathogens such as *Klebsiella-Aerobacter, Staph. aureus* and *Proteus mirabilis*.

Also effective in nonobstructed chronic and recurrent urinary tract infections

It is also common for the elderly and debilitated to develop chronic nonobstructed urinary tract infections, primarily pyelonephritis and cystitis. Such cases often respond satisfactorily to therapy with Gantanol.

B.I.D./T.I.D. schedule gives round-the-clock coverage

Subsequent 1-Gm doses can provide up to 12 hours of antibacterial activity. The *b.i.d.* dosage is recommended for mild to moderate infections; the *t.i.d.* for the more severe u.t.i. Gantanol provides coverage around the clock—coverage that is especially important during the hours of sleep, when urinary retention favors bacterial proliferation.

Your option: tablets or suspension

Gantanol is available in two convenient dosage forms—tablets or a pleasant-tasting suspension. It is generally well tolerated with relative freedom from complications. The usual precautions with sulfonamide therapy should be observed, including adequate fluid intake, frequent c.b.c.'s and urinalyses with microscopic examination. The most common side effects reported are nausea, vomiting and diarrhea. (It should also be noted that the increasing frequency of resistant organisms is a limitation of usefulness of antibacterial agents, including sulfonamides, especially in chronic or recurrent u.t.i.)

in nonobstructed pyelonephritis due to susceptible organisms

Gantanol®
(sulfamethoxazole)

Basic therapy

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Effective in acute, recurrent or chronic urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli, Klebsiella-Aerobacter, Staphylococcus aureus, Proteus mirabilis*, and, less frequently, *Proteus vulgaris*) and in the absence of obstructive uropathy or foreign bodies.

***Note:* Since *in vitro* sulfonamide sensitivity tests are not always reliable, carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response. Add aminobenzoic acid to culture media of patients receiving sulfonamides. The increasing frequency of resistant organisms is a limitation of usefulness of antibacterial agents, including sulfonamides, especially in chronic or recurrent urinary tract infections.**

Blood levels should be measured in patients receiving sulfonamides for serious infections, since there may be wide variations with identical doses; 20 mg/100 ml should be the maximum total sulfonamide level, as adverse reactions occur more frequently above this level.

Contraindications: Sulfonamide hypersensitivity; infants less than 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis); pregnancy at term and during nursing period.

Warnings: Safe use in pregnancy has not been established, and teratogenicity potential has not been thoroughly investigated. Sulfonamides will not eradicate or prevent sequelae to group A streptococcal infections, *i.e.*, rheumatic fever, glomerulonephritis. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported; early clinical signs such as sore throat, fever, pallor, purpura or jaundice may indicate serious blood disorders. Complete blood counts and urinalysis with careful microscopic examination are recommended frequently during sulfonamide therapy. Clinical data are insufficient on prolonged or recurrent therapy in chronic renal diseases of children under 6 years.

Precautions: Use with caution in patients with impaired renal or hepatic function, severe allergy, bronchial asthma and in glucose-6-phosphate dehydrogenase-deficient individuals. In the latter, dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias:* agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia; *allergic reactions:* erythema multiforme (Stevens-Johnson syndrome), skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis; *gastrointestinal reactions:* nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis; *C.N.S. reactions:* headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia; and *miscellaneous reactions:* drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon. Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide and thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age, except adjunctively with pyrimethamine in congenital toxoplasmosis. Usual dosage is as follows: *Adults*—2 Gm (4 tabs or teasp.) initially, then 1 Gm (2 tabs or teasp.) *b.i.d.* or *t.i.d.* depending on severity of infection. *Children*—0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially, followed by 0.25 Gm/20 lbs (½ tab or teasp.) *b.i.d.* Maximum dose for children should not exceed 75 mg/kg/24 hrs.

Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.

ROCHE
Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J 07110

Pinworm therapy is often a family affair





Contraindications: History of hypersensitivity to thiabendazole.
Warnings: If hypersensitivity reactions occur, drug should be discontinued immediately and not resumed. Rarely, erythema multiforme has been associated with thiabendazole therapy; in severe cases (Stevens-Johnson syndrome), fatalities have occurred. Because CNS side effects may occur quite frequently, activities requiring mental alertness should be avoided. Safe use in pregnancy or lactation has not been established.
Precautions: Ideally, supportive therapy is indicated for anemic, dehydrated, or malnourished patients prior to initiation of anthelmintic therapy. In presence of hepatic or renal dysfunction, patients should be carefully monitored.
Adverse Reactions: Most frequently encountered are anorexia, nausea, vomiting, and dizziness. Less frequently, diarrhea, epigastric distress, pruritus, weariness, drowsiness, giddiness, and headache have occurred. Rarely, tinnitus, hyperirritability, numbness, abnormal sensation in eyes, blurring of vision, xanthopsia; hypotension, collapse; enuresis; transient rise in cephalin flocculation and SGOT; perianal rash, cholestasis and parenchymal liver damage; hyperglycemia; transient leukopenia; malodor of the urine, crystalluria, hematuria; appearance of live Ascaris in the mouth and nose. Hypersensitivity reactions

A New Dosage Form:

Chewable Tablets 500 mg Mintezol®

(THIABENDAZOLE | MSD)



so easy to take everyone in the family will keep to the regimen you prescribe

include: fever, facial flush, chills, conjunctival injection, angioedema, anaphylaxis, skin rashes, erythema multiforme (including Stevens-Johnson syndrome), and lymphadenopathy.
Supplied: Chewable tablets, containing 500 mg thiabendazole, in boxes of 36, strip packaged, individually foil wrapped; Suspension, containing 500 mg thiabendazole per 5 cc, in bottles of 120 cc.

For more detailed information, consult your MSD representative or see the Direction Circular. Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa. 19486

MSD MERCK SHARP & DOHME

addendum

INDICATION | DOSAGE SCHEDULE

MINTEZOL® (Thiabendazole, MSD) has demonstrated effectiveness against a broad spectrum of nematode infestations, whether encountered singly or in combination. Dosages are weight related; therefore, a weight-dose chart is included in the Direction Circular for your convenience when writing a prescription. MINTEZOL should be given after meals if possible.

INDICATIONS	DOSAGE (1st Day)	ADDITIONAL REGIMEN	COMMENTS
Pinworm disease	Two doses of 1 tablet/50 lb	Repeat 7 days later	This regimen is designed to reduce the risk of reinfection. However, if not practical, repeat the regimen the next day.
Threadworm,* large roundworm,* hookworm,* and whipworm* disease	Two doses of 1 tablet/50 lb	Repeat the next day	Alternatively, a single dose of 2 tablets/50 lb may be given. However, a higher incidence of side effects should be expected.
Creeping eruption	Two doses of 1 tablet/50 lb	Repeat the next day	If active lesions are still present 2 days after completing this regimen, a second course is recommended.
Symptoms of trichinosis* during the invasive phase of the disease	Two doses of 1 tablet/50 lb	Repeat for 2 to 4 successive days	The optimal dosage for the treatment of trichinosis has not been established.

The recommended maximal daily dosage is 3 g (6 tablets).

*Clinical experience with thiabendazole for treatment of each of these conditions in children weighing less than 30 lb has been limited.

news

editorial

(Continued from Page 209)

where there are physician shortages.

6. Scholarships will be offered to students of medicine who agree, after completion of professional training, to engage in the practice of primary care in underserved areas.

7. Provisions are made for financial assistance in start-up operational costs for new schools of medicine, osteopathy and dentistry.

There are many sources of concern about this legislation. For example, it would seem appropriate to have more information about the results of education in three-year medical schools before a national policy is instituted. Both the Carnegie Commission Report and the Comprehensive Health Manpower Act focus on turning out an increased number of physicians, but direct little attention to the causes of maldistribution of health manpower. Despite this, every school of medicine in the United States is heavily dependent on the federal government for funds in order to carry out its mission. At the present time it is unlikely that a single medical school in this country has a choice except to accept the provisions of the legislation described above if that school is to survive.

There are obviously very serious implications in this entire matter for those concerned with medical education and the operation of the College of Medicine of the University of Oklahoma. One of the most serious concerns relates to the expansion of clinical facilities to provide training for this increased number of students. Another is the need to fund the expanded residency programs which will be needed to accommodate the greater number of graduates.

Early in the 1960's, the State Regents for Higher Education instructed the faculty of the University of Oklahoma Health Sciences Center to do a self-study of the educational needs of the state in the health professions. The results of the study were published and have influenced the course of health matters subsequently. The study called for better financial support for expansion of existing programs and enrollment, as well as for the establishment of new programs and new academic units. It also directed the center to develop a master plan for capital development. By 1969, all recommendations had been undertaken with varying degrees of success and completeness. The Medical Center has changed to the Health Sciences Center and the number of schools increased to six. The concept of an Oklahoma Health Center as a consortium of state, federal and private institutions having commitments to education, research and service has been developed and has gained nation-wide praise. The faculty of the College of Medicine developed a substantial revision of the curriculum, and the enrollment within the College of Medicine has been progressively increased. Despite all of these changes, which have been carried out in response to the directives of those official bodies responsible for higher education in Oklahoma, an additional fact has emerged clearly—no provision has been made, by those responsible, for a commensurate increase in the number of faculty and staff or in operational funds to meet these increased demands.

The press of the increased predoctoral student census is rendering the clinical facilities of the Health Sciences Center quantitatively inadequate. The number of clerkships, electives and other courses in community hospitals and other community health agencies is being increased. Such developments have logistic advantages for the volunteer clinical faculty in that they are able to teach where they are most at home. The experiences should be good for the students because their contacts are broadened with health problems and health delivery systems. The broadening of the base and community involvement throughout the state has important potential benefits. There are many problems, however, and all too often the individual faculty member or physician does not think these through carefully.

There are many urgent and fundamental questions which must be addressed. Some of these are:

What does the state of Oklahoma want? As outlined above, an ambitious program of expansion has been decreed by those responsible. Are these same individuals willing to provide the fiscal support to accomplish this?

How does the university health center obtain the capital and operational costs for this expanded number of students?

How much of the costs of residencies can be attributed to education and how much to service? Who pays the bill for each?

With the increasing number of students and the increased demands for delivery of health services, who will constitute the faculty responsible for satisfying these demands?

Who will be responsible for screening the content, supervising the teaching experience and "riding herd" on those immediately responsible for the instruction? Obviously, there cannot be "first class" and "second class" clerkships. The specific goals of the individual clerkships must be defined and a method of evaluation designed to judge their worth.

What is the role of the departmental chairman in the course or clerkship in question? Obviously, the clinical department chairman has innumerable and increasing demands on his time and cannot personally oversee the daily operation of each clerkship in every hospital. However, he is where the "buck" stops and he is regarded as ultimately responsible for the effectiveness of the educational program in his specialty.

What will be the role of the volunteer faculty in the design of these extramural offerings and what will be the relationships to the teaching experience and courses given on the health science center campus?

As in any other training experience, what will be the methods to objectively evaluate the performance of the student with an aim towards fortifying his strengths and improving his weaknesses?

The Health Sciences Center of the

DEATHS

RALPH A. McGILL, MD
1896-1972

A prominent Tulsa physician, Ralph A. McGill, MD, died April 30th, 1972. Doctor McGill was a Past-President of the Oklahoma State Medical Association, having served in 1950-51.

Born in Charlotte, Arkansas, Doctor McGill graduated from the University of Oklahoma School of Medicine in 1922. Specializing in general surgery, Doctor McGill had a special interest in tumor surgery and treatment. He helped found the Oklahoma Cancer Society and served as its President. He was a member of the Southwestern Surgical Congress and a Fellow of the American College of Surgeons and the International College of Surgeons.

Doctor McGill served as President of the Tulsa County Medical Society and was selected as "Doctor of the Year" by the Auxiliary to the Tulsa County Medical Society in 1969.

DONALD W. McCAULEY, MD
1917-1972

Donald W. McCauley, MD, Muskogee surgeon, died April 30th, 1972. Doctor McCauley had been in private practice in Okmulgee for twenty years before moving to Muskogee where he was a staff member of the Veterans Administration Hospital.

A native of Erie, Pennsylvania, Doctor McCauley was graduated from the University of Oklahoma School of Medicine in 1943. He was a member of the American College of Chest Physicians and the American College of Cardiology. □

University of Oklahoma has been and is being asked to take on increasing responsibilities in a variety of different areas relating to the production of health manpower and in the delivery of health services. The greatest pressure is on clinical departments and of these, by far the greatest is on so-called "primary" departments. Furthermore, the College of Medicine is being directed to provide quality education for this increased number of students and trainees in a compressed period of time.

The above-described demands are real because they stem from the needs of society and cannot be ignored. Faculty and staff of the Health Sciences Center are willing to accept these responsibilities. However, they can be met only if the state and the official groups responsible for higher education, specifically for education in the health-related fields, are willing to provide the necessary support. The time has come for a statement of priorities as to what the State of Oklahoma wants in health and health education.—*Harris D. Riley, Jr., MD.* □

Book Reviews

TOM RIVERS REFLECTIONS ON A LIFE IN MEDICINE AND SCIENCE. An oral history memoir prepared by Saul Benison. 682 pp. Cambridge: The M.I.T. Press. $17.50.

Doctor Thomas M. Rivers, one of the fathers of virology, died at the age of 73 in 1962. In the last few months of his life, this pioneer was persuaded by Doctor Saul Benison of Columbia University to collaborate in documention of his eventful career through the medium of oral history memoirs. The book is a record (edited only for reading convenience) of a series of tape recorded interviews. It is divided into 15 chapters with eight appendices.

Doctor Rivers was born in Georgia, was a graduate of the Johns Hopkins University School of Medicine and embarked on a career in pediatrics. Rivers proved to have a fine aptitude for clinical pediatrics and would probably have been destined for a distinguished career in this field had not World War I intervened. He was assigned to duty with the Army Pneumonia Board, which the Surgeon General had established to study the pneumonias complicating measles and influenza. He had been appointed to the board because of his aptitude in the clinical aspects of the infectious diseases. In this capacity he was closely associated with such distinguished investigators as Opie, Cole Blake and others; and it seems very likely that this exposure to experimental medical science influenced his decision to abandon clinical pediatrics in favor of the laboratory. In 1922 when Rivers went to the Rockefeller Institute to begin his studies in virus diseases, virology was not the robust science that it is today. As a young and untried investigator, Rivers entered a field of science that was also young and largely unprobed. He made many contributions and lived to see it become a mature and important science. The period spanned by Rivers' scientific career may truly be thought of as the "golden age of virology."

He became one of the leaders at the Rockefeller Institute for Medical Research. Following this, he served with the Naval Medical Research Unit, and in later years, with the Public Health Research Institute of New York and the National Foundation. He was instrumental in the successful development of oral poliovirus vaccine.

This memoir can in effect be regarded as a history of virology. It traces Doctor Rivers' personal investigative experience with smallpox, psittacosis, encephalitis, Rift Valley fever and other virus diseases. An analysis of Doctor Rivers' impact and role in contributing to the great development of virology and the tremendous increase in our knowledge concerning viruses and the diseases they cause is difficult to make because his influences were so numerous and so diverse and often quite subtle. However, if anyone can be said to have individually influenced the development of virology through its golden age of the past 30 years more than another, it is Rivers.

Although Doctor Rivers was by nature a friendly person, he had the capacity of being irascible and pug-

nacious. He was a difficult and formidable person to oppose and could be stubbornly inflexible in maintaining a position.

For those who had the privilege of knowing Doctor Rivers or who are interested in virology, this book will provide fascinating reading.—*Harris D. Riley, Jr., MD*

LASERS IN MEDICINE. By L. Goldman, BS, MD, Professor and Chairman, Department of Dermatology, and Director, Laser Laboratory, University of Cincinnati Medical Center, and R. J. Rockwell, Jr., BS, MSc, Associate Professor of Laser Sciences, Department of Dermatology, Otolaryngology, and Maxillofacial Surgery, and Directing Physicist, Laser Laboratory, University of Cincinnati Medical Center, Cincinnati, Ohio. 382 pp., with illustrations. New York: Gordon and Breach, 1971.

The development of laser (Light Amplification by Stimulated Emission of Radiation) devices has occurred with incredible speed since the first operational model was constructed in 1960. Reports on several hundred different laser systems have now been published, and the theoretical uses of this intense light beam have become of great interest to scientists in industry, the military, and medicine, as well as a source of fascination to the public. This publication contains extensive discussions of the general characteristics of laser devices and radiation as well as apparently thorough reviews of laser laboratory research. There are interesting chapters on holography and the use of the laser in cellular biology. The current roles of the laser in clinical medicine are relatively briefly discussed.

This book is not primarily intended for clinicians with only a routine premedical education. An excellent working knowledge of physics is necessary to fully understand and appreciate much of the publication, and this reviewer had more than a little difficulty following many of the discussions. The presentations are well organized and written, and extensive bibliographies are available at the end of each chapter.

Lasers are being used with increasing frequency in the field of ophthalmology, and the chapter on this subject is already quite significantly outdated. The authors have listed a wide variety of conditions which have been treated with the laser, but little data is presented to support the worth of such therapy. The true efficacy of laser photocoagulation in ophthalmology will remain unknown until control studies are available.

Physicians who are interested in laser physics or in basic research in the laser field should find this book valuable. For those interested in clinical studies assessing the value of the laser versus more traditional forms of management, this publication may prove disappointing. —*C. P. Wilkinson, MD* □

Miscellaneous Advertisements

INDUSTRIAL PHYSICIAN to assist a five-man department in large multi-specialty group. No plant responsibilities. Primary care of acute injuries. Must have one-year residency. Contact Joseph W. Rhine, P.O. Box 3718 or 918 742-3341.

PHYSICIANS WANTED. Planning to build multi-suite Professional Mall in Weatherford, Oklahoma, a friendly fast growing college city; will build to suit. Need Two MDs. Write T. J. Toma, DDS, Box 310, Weatherford 73096.

INTERNIST NEEDED in one of Oklahoma's fastest growing communities — Claremore. Seventy-five bed community hospital with plans to double in the next two years. Set your own schedule in this fine community. Office space available July 1st in new clinic. Mail inquiries to Drawer B, Claremore, Oklahoma 74017.

HEARING AID SUPPLIES for sale. Owner deceased. Audiometer, aids, cords, bone and air oscillators. Drastically reduced. Make offer after 5:30 p.m. Roger Sturgeon, 2023 North Shartel, Oklahoma City 405 525-3963.

OPPORTUNITY FOR GENERAL PRACTICE (with specialty interest if desired) in El Reno, a city of 15,000 only thirty minutes west of Oklahoma City. Established clinic of three doctors, adjacent to modern community hospital desires one or two associates for active group practice. Attractive salary and partnership opportunity. Let us show you a good deal. Contact Canadian Valley Clinic, 2001 Park View, El Reno, Oklahoma 73036 or call collect 405 262-2114, F. W. Hollingsworth, MD.

SURGEON LOOKING FOR LOCATION. Graduate of Paris Medical School; U.S. internship and residency; licensed in New York and Pennsylvania. Board eligible. Contact A. Sergie, MD, 113 Duncan Street, Dublin, Georgia 31021.

WOULD LIKE TO PURCHASE two used gynecological examining tables with matching cabinets, stools, trash cans, etc. Would pay one-half of original price if they are in fair condition. Might be interested in other used equipment. Contact Key S, The Journal, Oklahoma State Medical Association, 601 N.W. Expressway, Oklahoma City 73118.

FOR SALE: Used X-ray machine, Profexray. Also other items for doctor's clinic. Call or write Billings Chamber of Commerce, c/o Aubrey Tipton, Billings, Oklahoma 74630. Phone 725-3424. □



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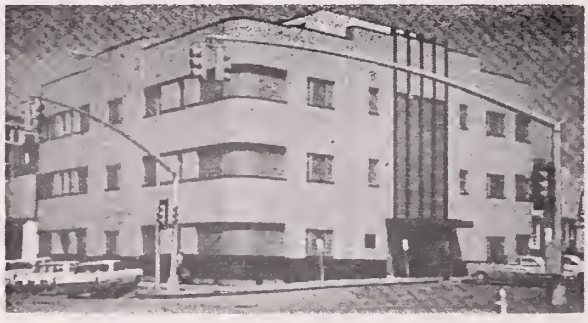
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Pre-Sate®
(chlorphentermine HCl)

CAUTION: Federal law prohibits dispensing without prescription.

Indications: Pre-Sate (chlorphentermine hydrochloride) is indicated in exogenous obesity, as a short term (*i.e.*, several weeks) adjunct in a regimen of weight reduction based upon caloric restriction.

Contraindications: Glaucoma, hyperthyroidism, pheochromocytoma, hypersensitivity to sympathomimetic amines, and agitated states. Pre-Sate (chlorphentermine hydrochloride) is also contraindicated in patients with a history of drug abuse or symptomatic cardiovascular disease of the following types: advanced arteriosclerosis, severe coronary artery disease, moderate to severe hypertension, or cardiac conduction abnormalities with danger of arrhythmias. The drug is also contraindicated during or within 14 days following administration of monamine oxidase inhibitors, since hypertensive crises may result.

Warnings: When weight loss is unsatisfactory the recommended dosage should not be increased in an attempt to obtain increased anorexigenic effect; discontinue the drug. Tolerance to the anorectic effect may develop. Drowsiness or stimulation may occur and may impair ability to engage in potentially hazardous activities such as operating machinery, driving a motor vehicle, or performing tasks requiring precision work or critical judgment. Therefore, such patients should be cautioned accordingly. Caution must be exercised if Pre-Sate (chlorphentermine hydrochloride) is used concomitantly with other central nervous system stimulants. There have been reports of pulmonary hypertension in patients who received related drugs.

Drug Dependence: Drugs of this type have a potential for abuse. Patients have been known to increase the intake of drugs of this type to many times the dosages recommended. In long-term controlled studies with high dosages of Pre-Sate, abrupt cessation did not result in symptoms of withdrawal.

Usage In Pregnancy: The safety of Pre-Sate (chlorphentermine hydrochloride) in human pregnancy has not yet been clearly established. The use of anorectic agents by women who are or who may become pregnant, and especially those in the first trimester of pregnancy, requires that the potential benefit be weighed against the possible hazard to mother and child. Use of the drug during lactation is not recommended. Mammalian reproductive and teratogenic studies with high multiples of the human dose have been negative.

Usage In Children: Not recommended for use in children under 12 years of age.

Precautions: In patients with diabetes mellitus there may be alteration of insulin requirements due to dietary restrictions and weight loss. Pre-Sate (chlorphentermine hydrochloride) should be used with caution when obesity complicates the management of patients with mild to moderate cardiovascular disease or diabetes mellitus, and only when dietary restriction alone has been unsuccessful in achieving desired weight reduction. In prescribing this drug for obese patients in whom it is undesirable to introduce CNS stimulation or pressor effect, the physician should be alert to the individual who may be overly sensitive to this drug. Psychologic disturbances have been reported in patients who concomitantly receive an anorexic agent and a restrictive dietary regimen.

Adverse Reactions: Central Nervous System: When CNS side effects occur, they are most often manifested as drowsiness or sedation or overstimulation and restlessness. Insomnia, dizziness, headache, euphoria, dysphoria, and tremor may also occur. Psychotic episodes, although rare, have been noted even at recommended doses. **Cardiovascular:** tachycardia, palpitation, elevation of blood pressure. **Gastrointestinal:** nausea and vomiting, diarrhea, unpleasant taste, constipation. **Endocrine:** changes in libido, impotence. **Autonomic:** dryness of mouth, sweating, mydriasis. **Allergic:** urticaria. **Genitourinary:** diuresis and, rarely, difficulty in initiating micturition. **Others:** Paresthesias, sural spasms.

Dosage and Administration: The recommended adult daily dose of Pre-Sate (chlorphentermine hydrochloride) is one tablet (equivalent to 65 mg chlorphentermine base) taken after the first meal of the day. Use in children under 12 not recommended.

Overdosage: Manifestations: Restlessness, confusion, assaultiveness, hallucinations, panic states, and hyperpyrexia may be manifestations of acute intoxication with anorectic agents. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension, or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Fatal poisoning usually terminates in convulsions and coma.

Management: Management of acute intoxication with sympathomimetic amines is largely symptomatic and supportive and often includes sedation with a barbiturate. If hypertension is marked, the use of a nitrate or rapidly acting alpha-receptor blocking agent should be considered. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendations in this regard.

How Supplied: Each Pre-Sate (chlorphentermine hydrochloride) tablet contains the equivalent of 65 mg chlorphentermine base; bottles of 100 and 1000 tablets.

Full information available on request.

WC **WARNER-CHILCOTT**
Division, Warner-Lambert Company
Morris Plains, New Jersey 07950



Pre-Sate® (chlorphentermine HCl)...the increasingly practical appetite suppressant



When you select this familiar antibiotic for IV infusion you have available a broad dosage range that hospitalized patients may need.

Intravenous Lincocin (lincomycin hydrochloride, Upjohn), with its 1.2 to 8 grams/day dosage range, covers many serious and even life-threatening infections. Lincocin is effective in infections due to susceptible strains of streptococci, pneumococci, and staphylococci. Lincocin IV therefore can be as useful in your hospitalized patients as its IM use has proved to be in your office patients. As with all antibiotics, *in vitro* susceptibility studies should be performed.

1.2 to 8 grams/day IV dosage range: Most hospitalized patients with uncomplicated pneumonias respond satisfactorily to 1.2 to 1.8 grams/day of Lincocin IV. These doses may have to be increased for more serious infections. In life-threatening situations as much as 8 grams/day has been administered intravenously to adults.

In usual IV doses, Lincocin (lincomycin hydrochloride, Upjohn) should be diluted in 250 ml or more of normal saline solution or 5% glucose in water. But when 4 grams or more per day is given, Lincocin should be diluted in not less than 500 ml of either solution, and the rate of administration should not exceed 100 ml/hour. Too rapid intravenous administration of doses exceeding 4 grams may result in hypotension or, in rare instances, cardiopulmonary arrest.

Effective gram-positive antibiotic: Lincocin IV is effective in respiratory tract, skin and soft-tissue, and bone

infections caused by susceptible strains of pneumococci, streptococci, and staphylococci, including penicillin-resistant strains. Staphylococcal strains resistant to Lincocin (lincomycin hydrochloride, Upjohn) have been recovered. Before initiating therapy, culture and susceptibility studies should be performed. Lincocin has proved valuable in treating patients hypersensitive to penicillin or cephalosporins, since Lincocin does not share antigenicity with these compounds. However, hypersensitivity reactions have been reported, some of these in patients known to be sensitive to penicillin.

Well tolerated at infusion site: Lincocin intravenous infusions have not produced local irritation or phlebitis, when given as recommended. Lincocin is usually well tolerated in patients who are hypersensitive to other drugs. Nevertheless, Lincocin should be used cautiously in patients with asthma or significant allergies.

In patients with impaired renal function, the recommended dose of Lincocin should be reduced to 25—30% of the dose for patients with normal kidney function. Its safety in pregnant patients and in infants less than one month of age has not been established.

Lincocin may be used with other antimicrobial agents: Since Lincocin is stable over a wide pH range, it is suitable for incorporation in intravenous infusions; it also may be administered concomitantly with other antimicrobial agents when indicated. However, Lincocin should not be used with erythromycin, as *in vitro* antagonism has been reported.

Lincocin®

Sterile Solution (300 mg per ml)

(lincomycin hydrochloride, Upjohn)

For further prescribing information, please see following page.



© 1972 The Upjohn Company



Sterile Solution (300 mg. per ml.)

Lincocin®

(lincomycin hydrochloride, Upjohn)

Up to 8 grams per day by IV infusion for hospitalized patients with life-threatening infections. Lincocin is effective in infections due to susceptible strains of streptococci, pneumococci, and staphylococci. As with all antibiotics, *in vitro* susceptibility studies should be performed.

Each preparation contains:	Lincomycin hydrochloride monohydrate equivalent to lincomycin base
250 mg Pediatric Capsule	250 mg
500 mg Capsule	500 mg
*Sterile Solution per 1 ml	300 mg
Syrup per 5 ml	250 mg

*Contains also: Benzyl Alcohol 9 mg; and, Water for Injection—q.s.

Lincocin (lincomycin hydrochloride) is indicated in infections due to susceptible strains of staphylococci, pneumococci, and streptococci. *In vitro* susceptibility studies should be performed. Cross resistance has not been demonstrated with penicillin, ampicillin, cephalosporins, chloramphenicol or the tetracyclines. Some cross resistance with erythromycin has been reported. Studies indicate that Lincocin does not share antigenicity with penicillin compounds.

CONTRAINDICATIONS: History of prior hypersensitivity to lincomycin or clindamycin. Not indicated in the treatment of viral or minor bacterial infections.

WARNINGS: *CASES OF SEVERE AND PERSISTENT DIARRHEA HAVE BEEN REPORTED AND HAVE AT TIMES NECESSITATED DISCONTINUANCE OF THE DRUG. THIS DIARRHEA HAS BEEN OCCASIONALLY ASSOCIATED WITH BLOOD AND MUCUS IN THE STOOLS AND HAS AT TIMES RESULTED IN AN ACUTE COLITIS. THIS SIDE EFFECT USUALLY HAS BEEN ASSOCIATED WITH THE ORAL DOSAGE FORM BUT OCCASIONALLY HAS BEEN REPORTED FOLLOWING PARENTERAL THERAPY.* A careful inquiry should be made concerning previous sensitivities to drugs or other allergens. Safety for use in pregnancy has not been established and Lincocin (lincomycin hydrochloride) is not indicated in the newborn. Reduce dose 25 to 30% in patients with severe impairment of renal function.

PRECAUTIONS: Like any drug, Lincocin should be used with caution in patients having a history of asthma or significant allergies. Overgrowth of nonsusceptible organisms, particularly yeasts, may occur and require appropriate measures. Patients with pre-existing monilial infections requiring Lincocin therapy should be given concomitant antimonilial treatment. During prolonged Lincocin therapy, periodic liver function studies and blood counts should be performed. Not recommended (inadequate data) in patients with pre-existing liver disease unless special clinical circumstances indicate. Continue treatment of β-hemolytic streptococci infections for 10 days to diminish likelihood of rheumatic fever or glomerulonephritis.

ADVERSE REACTIONS: *Gastrointestinal*—Glossitis, stomatitis, nausea, vomiting. Persistent diarrhea, enterocolitis, and pruritus ani. *Hemopoietic*—Neutropenia, leukopenia, agranulocytosis, and thrombocytopenic purpura have been reported. *Hypersensitivity reactions*—Hypersensitivity reactions such as angioneurotic edema, serum sickness, and anaphylaxis have been reported, sometimes in patients sensitive to penicillin. If allergic reaction occurs, discontinue drug. Have epinephrine, corticosteroids, and antihistamines available for emergency treatment. *Skin and mucous membranes*—Skin rashes, urticaria, vaginitis, and rare instances of exfoliative and vesiculobullous dermatitis have been reported. *Liver*—Although no direct relationship to liver dysfunction is established, jaundice and abnormal liver function tests (particularly serum transaminase) have been observed in a few instances. *Cardiovascular*—Instances of hypotension following parenteral administration have been reported, particularly after too rapid IV administration. Rare instances of cardiopulmonary arrest have been reported after too rapid IV administration. If 4.0 grams or more administered IV, dilute in 500 ml of fluid and administer no faster than 100 ml per hour. *Special senses*—Tinnitus and vertigo have been reported occasionally. *Local reactions*—Excellent local tolerance demonstrated to intramuscularly administered Lincocin (lincomycin hydrochloride). Reports of pain following injection have been infrequent. Intravenous administration of Lincocin in 250 to 500 ml of 5% glucose in distilled water or normal saline has produced no local irritation or phlebitis.

HOW SUPPLIED: *250 mg* and *500 mg* Capsules—bottles of 24 and 100. *Sterile Solution, 300 mg per ml*—2 and 10 ml vials and 2 ml syringe. *Syrup, 250 mg per 5 ml*—60 ml and pint bottles.

For additional product information, consult the package insert or see your Upjohn representative.

MED B-6-S (KZL-7) JA71-1631

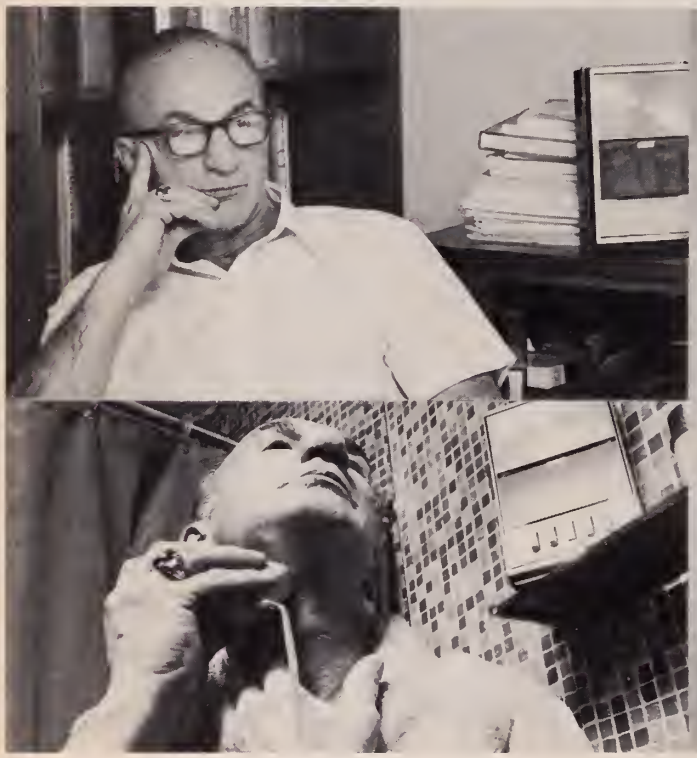
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Kalamazoo, Michigan 49001

Upjohn


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rheumatoid arthritic blowup...

Tandearil® Geigy

oxyphenbutazone NF

tablets of 100 mg.

Important Note: This drug is not a simple analgesic. Do not administer casually. Carefully evaluate patients before starting treatment and keep them under close supervision. Obtain a detailed history, and complete physical and laboratory examination (complete hemogram, urinalysis, etc.) before prescribing and at frequent intervals thereafter. Carefully select patients, avoiding those responsive to routine measures, contraindicated patients or those who cannot be observed frequently. Warn patients not to exceed recommended dosage. Short-term relief of severe symptoms with the smallest possible dosage is the goal of therapy. Dosage should be taken with meals or a full glass of milk. Patients should discontinue the drug and report immediately any sign of: fever, sore throat, oral lesions (symptoms of blood dyscrasia); dyspepsia, epigastric pain, symptoms of anemia, black or tarry stools or other evidence of intestinal ulceration or hemorrhage, skin reactions, significant weight gain or edema. A one-week trial period is adequate. Discontinue in the absence of a favorable response. Restrict treatment periods to one week in patients over sixty.
Indications: Acute gouty arthritis, rheumatoid arthritis, rheumatoid spondylitis.
Contraindications: Children 14 years or less; senile patients; history or symptoms of G.I. inflammation or ulceration including severe, recurrent or persistent dyspepsia; history or presence of drug allergy; blood dyscrasias; renal, hepatic or cardiac dysfunction; hypertension; thyroid disease; systemic edema; stomatitis and salivary gland enlargement due to the drug; polymyalgia rheumatica and temporal arteritis; patients receiving other potent chemotherapeutic agents, or long-term anticoagulant therapy.
Warnings: Age, weight, dosage, duration of therapy, existence of concomitant diseases, and concurrent potent chemotherapy affect incidence of toxic reactions. Carefully instruct and observe the individual patient, especially the aging (forty years and over) who have increased susceptibility to the toxicity of the drug. Use lowest effective dosage. Weigh initially unpredictable benefits against potential risk of severe, even fatal, reactions. The disease condition itself is unaltered by the drug. Use with caution in first trimester of pregnancy and in nursing mothers. Drug may appear in cord blood and breast milk. Serious, even fatal, blood dyscrasias, including aplastic anemia, may occur suddenly despite regular hemograms, and may become manifest days or weeks after cessation of drug. Any significant change in total white count, relative decrease in granulocytes, appearance of immature forms, or fall in hematocrit should signal immediate cessation of therapy and complete hematologic investigation. Unexplained bleeding involving CNS, adrenals, and G.I. tract has occurred. The drug may potentiate action of insulin, sulfonylurea, and sulfonamide-type agents. Carefully observe patients taking these agents. Nontoxic and toxic goiters and myxedema have been reported (the drug reduces iodine uptake by the thyroid). Blurred vision can be a significant toxic symptom worthy of a complete ophthalmological examination. Swelling of ankles or face in patients under sixty may be prevented by reducing dosage. If edema occurs in patients over sixty, discontinue drug.
Precautions: The following should be accomplished at regular intervals: Careful detailed history for disease being treated and detection of earliest signs of adverse reactions; complete physical examination including check of patient's weight; complete weekly (especially for the aging) or an every two week blood check; pertinent laboratory studies. Caution patients about participating in activity requiring alertness and coordination, as driving a car, etc. Cases of leukemia have been reported in patients with a history of short- and long-term therapy. The majority of these patients were over forty. Remember that arthritic-type pains can be the presenting symptom of leukemia.
Adverse Reactions: This is a potent drug; its misuse can lead to serious results. Review detailed information before beginning therapy. Ulcerative esophagitis, acute and reactivated gastric and duodenal ulcer with perforation and hemorrhage, ulceration and perforation of large bowel, occult G.I. bleeding with anemia, gastritis, epigastric pain, hematemesis, dyspepsia, nausea, vomiting and diarrhea, abdominal distention, agranulocytosis, aplastic anemia, hemolytic anemia, anemia due to blood loss including occult G.I. bleeding, thrombocytopenia, pancytopenia, leukemia, leukopenia, bone marrow depression, sodium and chloride retention, water retention and edema, plasma dilution, respiratory alkalosis, metabolic acidosis, fatal and nonfatal hepatitis (cholestasis may or may not be prominent), petechiae, purpura without thrombocytopenia, toxic pruritus, erythema nodosum, erythema multiforme, Stevens-Johnson syndrome, Lyell's syndrome (toxic necrotizing epidermolysis), exfoliative dermatitis, serum sickness, hypersensitivity angiitis (polyarteritis), anaphylactic shock, urticaria, arthralgia, fever, rashes (all allergic reactions require prompt and permanent withdrawal of the drug), proteinuria, hematuria, oliguria, anuria, renal failure with azotemia, glomerulonephritis, acute tubular necrosis, nephrotic syndrome, bilateral renal cortical necrosis, renal stones, ureteral obstruction with uric acid crystals due to uricosuric action of drug, impaired renal function, cardiac decompensation, hypertension, pericarditis, diffuse interstitial myocarditis with muscle necrosis, perivascular granulomata, aggravation of temporal arteritis in patients with polymyalgia rheumatica, optic neuritis, blurred vision, retinal hemorrhage, toxic amblyopia, retinal detachment, hearing loss, hyperglycemia, thyroid hyperplasia, toxic goiter association of hyperthyroidism and hypothyroidism (causal relationship not established), agitation, confusional states, lethargy; CNS reactions associated with overdosage, including convulsions, euphoria, psychosis, depression, headaches, hallucinations, giddiness, vertigo, coma, hyperventilation, insomnia; ulcerative stomatitis, salivary gland enlargement.
(B) 98-146-800-E

For complete details, including dosage, please see full prescribing information.

GEIGY Pharmaceuticals
Division of CIBA-GEIGY Corporation
Ardsley, New York 10502

TA.8356-9



if skin is infected, or open to infection...

choose the topicals that give your patient–

- broad antibacterial activity against susceptible skin invaders
- low allergenic risk—prompt clinical response

Special Petrolatum Base
Neosporin® Ointment
(polymyxin B-bacitracin-neomycin)

Each gram contains: Aerosporin® brand polymyxin B sulfate, 5000 units; zinc bacitracin, 400 units; neomycin sulfate 5 mg. (equivalent to 3.5 mg. neomycin base); special white petrolatum q. s.
In tubes of 1 oz. and ½ oz. for topical use only.

Vanishing Cream Base
Neosporin®-G Cream
(polymyxin B-neomycin-gramicidin)

Each gram contains: Aerosporin® brand polymyxin B sulfate, 10,000 units; neomycin sulfate, 5 mg. (equivalent to 3.5 mg. neomycin base); gramicidin, 0.25 mg., in a smooth, white, water-washable vanishing cream base with a pH of approximately 5.0. Inactive ingredients: liquid petrolatum, white petrolatum, propylene glycol, polyoxyethylene polyoxypropylene compound, emulsifying wax, purified water, and 0.25% methylparaben as preservative.
In tubes of 15 g.

NEOSPORIN for topical infections due to susceptible organisms, as in impetigo, surgical after-care, and pyogenic dermatoses.

Precaution: As with other antibiotic preparations, prolonged use may result in overgrowth of nonsusceptible organisms and/or fungi. Appropriate measures should be taken if this occurs. Articles in the current medical literature indicate an increase in the prevalence of persons allergic to neomycin. The possibility of such a reaction should be borne in mind.

Contraindications: Not for use in the external ear canal if the eardrum is perforated. These products are contraindicated in those individuals who have shown hypersensitivity to any of the components.

Complete literature available on request from Professional Services Dept. PML.

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Research Triangle Park
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He won't resist feeling better with Mylanta®

Because the taste is good.

- ☐ promptly relieves hyperacidity
- ☐ also relieves fullness and bloating
- ☐ non-constipating



LIQUID **MYLANTA**® TABLETS

aluminum and magnesium hydroxides with simethicone

STUART PHARMACEUTICALS | Division of ICI America Inc. | Wilmington, Del. 19899 | Pasadena, Calif. 91109



a new outlook in chronic pain

of moderate to severe intensity

Though Talwin® can be compared to codeine in analgesic efficacy, it is not a narcotic. So patients receiving Talwin for prolonged periods face fewer of the consequences you've come to expect with narcotic analgesics. And that, in the long run, can mean a better outlook for your chronic-pain patient.

Talwin Tablets are:

- **Comparable to codeine in analgesic efficacy:** one 50 mg. Talwin Tablet appears equivalent in analgesic effect to 60 mg. (1 gr.) of codeine. Onset of significant analgesia usually occurs within 15 to 30 minutes. Analgesia is usually maintained for 3 hours or longer.
- **Tolerance not a problem:** tolerance to the analgesic effect of Talwin Tablets has not been reported, and no significant changes in clinical laboratory parameters attributable to the drug have been reported.
- **Dependence rarely a problem:** during three years of wide clinical use, only a few cases of dependence have been reported. In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in dose by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain.
- **Not subject to narcotic controls:** convenient to prescribe—day or night—even by phone.
- **Generally well tolerated by most patients:** infrequently cause decrease in blood pressure or tachycardia; rarely cause respiratory depression or urinary retention; seldom cause diarrhea or constipation. If dizziness, lightheadedness, nausea or vomiting are encountered, these effects tend to be self-limiting and to decrease after the first few doses. (See last page of this advertisement for a complete discussion of adverse reactions and a brief discussion of other Prescribing Information.)

50 mg. Tablets

Talwin®

brand of

pentazocine (as hydrochloride)

the long-range analgesic

a new outlook in chronic pain

of moderate to severe intensity



Contraindications: Talwin, brand of pentazocine (as hydrochloride), should not be administered to patients who are hypersensitive to it.

Warnings: *Head Injury and Increased Intracranial Pressure.* The respiratory depressant effects of Talwin and its potential for elevating cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a preexisting increase in intracranial pressure. Furthermore, Talwin can produce effects which may obscure the clinical course of patients with head injuries. In such patients, Talwin must be used with extreme caution and only if its use is deemed essential.

Usage in Pregnancy. Safe use of Talwin during pregnancy (other than labor) has not been established. Animal reproduction studies have not demonstrated teratogenic or embryotoxic effects. However, Talwin should be administered to pregnant patients (other than labor) only when, in the judgment of the physician, the potential benefits outweigh the possible hazards. Patients receiving Talwin during labor have experienced no adverse effects other than those that occur with commonly used analgesics. Talwin should be used with caution in women delivering premature infants.

Drug Dependence. There have been instances of psychological and physical dependence on parenteral Talwin in patients with a history of drug abuse and, rarely, in patients without such a history. Abrupt discontinuance following the extended use of parenteral Talwin has resulted in withdrawal symptoms. There have been a few reports of dependence and of withdrawal symptoms with orally administered Talwin. Patients with a history of drug dependence should be under close supervision while receiving Talwin orally.

In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in dose by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain.

Acute CNS Manifestations. Patients receiving therapeutic doses of Talwin have experienced, in rare instances, hallucinations (usually visual), disorientation, and confusion which have cleared spontaneously within a period of hours. The mechanism of this reaction is not known. Such patients should be very closely observed and vital signs checked. If the drug is reinstituted it should be done with caution since the acute CNS manifestations may recur.

Usage in Children. Because clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Ambulatory Patients. Since sedation, dizziness, and occasional euphoria have been noted, ambulatory patients should be warned not to operate machinery, drive cars, or unnecessarily expose themselves to hazards.

Precautions: *Certain Respiratory Conditions.* Although respiratory depression has rarely been reported after oral administration of Talwin, the drug should be administered with caution to patients with respiratory depression from any cause, severe bronchial asthma and other obstructive respiratory conditions, or cyanosis.

Impaired Renal or Hepatic Function. Decreased metabolism of the drug by the liver in extensive liver disease may predispose to accentuation of side effects. Although laboratory tests have not indicated that Talwin causes or increases renal or hepatic impairment, the drug should be administered with caution to patients with such impairment.

Myocardial Infarction. As with all drugs, Talwin should be used with caution in patients with myocardial infarction who have nausea or vomiting.

Biliary Surgery. Until further experience is gained with the effects of Talwin on the sphincter of Oddi, the drug should be used with caution in patients about to undergo surgery of the biliary tract.

Patients Receiving Narcotics. Talwin is a mild narcotic antagonist. Some patients previously receiving narcotics have experienced mild withdrawal symptoms after receiving Talwin.

CNS Effect. Caution should be used when Talwin is administered to patients prone to seizures; seizures have occurred in a few such patients in association with the use of Talwin although no cause and effect relationship has been established.

Adverse Reactions: Reactions reported after oral administration of Talwin include *gastrointestinal:* nausea, vomiting; infrequently constipation; and rarely abdominal distress, anorexia, diarrhea. *CNS effects:* dizziness, lightheadedness, sedation, euphoria, headache; infrequently weakness, disturbed dreams, insomnia, syncope, visual blurring and focusing difficulty, hallucinations (see *Acute CNS Manifestations* under WARNINGS); and rarely tremor, irritability, excitement, tinnitus. *Autonomic:* sweating; infrequently flushing; and rarely chills. *Allergic:* infrequently rash; and rarely urticaria, edema of the face. *Cardiovascular:* infrequently decrease in blood pressure, tachycardia. *Other:* rarely respiratory depression, urinary retention.

Dosage and Administration: *Adults.* The usual initial adult dose is 1 tablet (50 mg.) every three or four hours. This may be increased to 2 tablets (100 mg.) when needed. Total daily dosage should not exceed 600 mg.

When antiinflammatory or antipyretic effects are desired in addition to analgesia, aspirin can be administered concomitantly with Talwin.

Children Under 12 Years of Age. Since clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Duration of Therapy. Patients with chronic pain who have received Talwin orally for prolonged periods have not experienced withdrawal symptoms even when administration was abruptly discontinued (see WARNINGS). No tolerance to the analgesic effect has been observed. Laboratory tests of blood and urine and of liver and kidney function have revealed no significant abnormalities after prolonged administration of Talwin.

Overdosage: *Manifestations.* Clinical experience with Talwin overdosage has been insufficient to define the signs of this condition.

Treatment. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated. Assisted or controlled ventilation should also be considered. Although nalorphine and levallorphan are *not* effective antidotes for respiratory depression due to overdosage or unusual sensitivity to Talwin, parenteral naloxone (Narcan®, available through Endo Laboratories) is a specific and effective antagonist. If naloxone is not available, parenteral administration of the analeptic, methylphenidate (Ritalin®), may be of value if respiratory depression occurs.

Talwin is not subject to narcotic controls.

How Supplied: Tablets, peach color, scored. Each tablet contains Talwin (brand of pentazocine) as hydrochloride equivalent to 50 mg. base. Bottles of 100.

Winthrop Winthrop Laboratories, New York, N. Y. 10016 (1583)

50 mg. Tablets

Talwin®

brand of

pentazocine (as hydrochloride)

the long-range analgesic

140/90 is normal blood pressure...or is it?

An extensive study based on nearly 4 million life insurance policies suggests that a blood pressure reading of 140/90 requires close medical supervision.

Study Findings. Twelve years ago the Society of Actuaries reported on an extensive study based on the lives and deaths represented by almost 4 million life insurance policies. From this vast survey—"The Build and Blood Pressure Study"[1]—insurance experts concluded that:

- Blood pressure above 140/90 is accompanied by increased morbidity and requires close medical attention.
- Even small increments in either systolic or diastolic blood pressure progressively and steeply shorten life expectancy.

Other Studies. Studies conducted with large numbers of patients since that time have echoed the above findings. Two studies published in 1970—the VA Cooperative Study Group on "Effects of Treatment on Morbidity in Hypertension"[2] and the "Framingham Study"[3]—suggest that treatment of even mild hypertension may, over time, offer significant benefits to the patient.

Another Point of View. Although a growing body of studies suggests that treatment of mild hypertension is warranted, medical opinion is not unanimous. Some clinicians recommend that drug treatment for mild hypertension be reserved for patients with additional risk factors such as smoking, high cholesterol levels, heart or kidney involvement, or a family history of vascular disease. Dr. Walter M. Kirkendall stated this position in his recent paper "What's With Hypertension These Days?"[4] Discussing the management of hypertension in patients with a sustained diastolic pressure up to 100 mm Hg, he said: "Generally, I do not recommend antihypertensive therapy unless patient's blood pressure approaches the upper limit for the group and a number of adverse factors exist, such as male sex, family history of vascular disease, youth, evidence of heart or kidney involvement."



Drug Therapy for Hypertension. Although opinion varies on when to start drug therapy for mild hypertension, many physicians agree that treatment should start with a thiazide diuretic such as HydroDIURIL. For the adult patient, the usual starting dosage is 50 mg b.i.d. Dosage adjustments are recommended as the patient responds to treatment. The patient whose therapy begins with HydroDIURIL frequently can continue to benefit from it, because HydroDIURIL usually maintains its antihypertensive effect even when therapy is prolonged.

MSD
MERCK SHARP & DOHME

25- and 50-mg tablets

HydroDIURIL®

(Hydrochlorothiazide|MSD)

Therapy to Start With

For a brief summary of prescribing information, please see next page.

1. Society of Actuaries, *The Build and Blood Pressure Study*, 1959.
2. Veterans Administration Cooperative Study Group on Antihypertensive Agents, "Effects of Treatment on Morbidity in Hypertension," JAMA *213*:1143-1152, Aug. 17, 1970.
3. Kannel, William B., *et al.*: "Epidemiologic Assessment of the Role of Blood Pressure in Stroke—The Framingham Study," JAMA *214*:301-310, Oct. 12, 1970.
4. Kirkendall, Walter M.: "What's With Hypertension These Days?" Consultant, Jan. 1971.

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Therapy to Start With

Drug Therapy for Hypertension. Although opinion varies on when to start drug therapy for mild hypertension, many physicians agree that treatment should start with a thiazide diuretic such as HydroDIURIL. For the adult patient, the usual starting dosage is 50 mg b.i.d. Dosage adjustments are recommended as the patient responds to treatment. The patient whose therapy begins with HydroDIURIL frequently can continue to benefit from it, because HydroDIURIL usually maintains its antihypertensive effect even when therapy is prolonged.

CONTRAINDICATIONS: Anuria; increasing azotemia and oliguria during treatment of severe progressive renal disease. Known sensitivity to this compound. Nursing mothers; if use of drug is deemed essential, patient should stop nursing.

WARNINGS: May precipitate or increase azotemia. Use special caution in impaired renal function to avoid cumulative or toxic effects. Minor alterations of fluid and electrolyte balance may precipitate coma in hepatic cirrhosis.

When used with other antihypertensive drugs, careful observation for changes in blood pressure must be made, especially during initial therapy. Dosage of other antihypertensive agents, especially ganglion blockers, must be reduced by at least 50% because HydroDIURIL potentiates their action.

Stenosis and ulceration of the small bowel causing obstruction, hemorrhage, and perforation have been reported with the use of enteric-coated potassium tablets, either alone or with nonenteric-coated thiazides. Surgery was frequently required, and deaths have occurred. Such formulations should be used only when indicated and when dietary supplementation is impractical. Discontinue immediately if abdominal pain, distention, nausea, vomiting, or gastrointestinal bleeding occurs.

Thiazides cross placenta and appear in cord blood. In women of childbearing age, potential benefits must be weighed against possible hazards to fetus, such as fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

The possibility of sensitivity reactions should be considered in patients with a history of allergy or bronchial asthma. The possibility of exacerbation or activation of systemic lupus erythematosus has been reported for sulfonamide derivatives, including thiazides.

PRECAUTIONS: Check for signs of fluid and electrolyte imbalance, particularly if vomiting is excessive or patient is receiving parenteral fluids. Warning signs, irrespective of cause, are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances. Hypokalemia may develop (especially with brisk diuresis) in severe cirrhosis; with concomitant steroid or ACTH therapy; or with inadequate electrolyte intake. Digitalis therapy may exaggerate metabolic effects of hypokalemia, especially with reference to myocardial activity. Hypokalemia may be avoided or treated by use of potassium chloride or giving foods with a high potassium content. Similarly, any chloride deficit may be corrected by use of ammonium chloride (except in patients with hepatic disease) and largely prevented by a near normal salt intake. Hypochloremic alkalosis occurs infrequently and is rarely severe. In severely edematous patients with congestive failure or renal disease, a low salt syndrome may occur if dietary salt is unduly restricted, especially during hot weather.

Thiazides may increase responsiveness to tubocurarine. The antihypertensive effect of the drug may be enhanced in the postsympathectomy patient. Arterial responsiveness to norepinephrine is decreased, necessitating care in surgical patients. Discontinue drug 48 hours before elective surgery. Orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics.

Pathological changes in the parathyroid glands with hypercalcemia and hypophosphatemia have been seen in a few patients on prolonged thiazide therapy. The effect of discontinuing thiazide therapy on serum calcium and phosphorus levels may be helpful in assessing the need for parathyroid surgery in such patients. Parathyroidectomy has elicited subjective clinical improvement in most patients, but has no effect on hypertension. Thiazide therapy may be resumed after surgery.

Use cautiously in hyperuricemic or gouty patients; gout may be precipitated. May affect insulin requirements in diabetics; may induce hyperglycemia and glycosuria in latent diabetics.

ADVERSE REACTIONS: Rare reactions include thrombocytopenia, leukopenia, agranulocytosis, aplastic anemia, cholestasis, and pericholangiolitic hepatitis. Nausea, vomiting, diarrhea, dizziness, vertigo, paresthesias, transient blurred vision, sialadenitis, purpura, rash, urticaria, photosensitivity, or other hypersensitivity reactions may occur. Cutaneous vasculitis precipitated by thiazide diuretics has been reported in elderly patients on repeated and continuing exposure to several drugs. Scattered reports have linked thiazides to pancreatitis, xanthopsia, neonatal thrombocytopenia, and neonatal jaundice. When adverse reactions are moderate or severe, the dosage of thiazides should be reduced or therapy withdrawn.

For more detailed information, consult your MSD Representative or see the Direction Circular. Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa. 19486

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Prompt relief of pain is a lot of what the practice of medicine is all about...East or West.

In much of the Far East, the analgesic efficacy of Empirin® Compound with Codeine would probably be measured against acupuncture, an ancient and traditional therapeutic system.

In America, codeine sets such a high standard for oral analgesia, that it has become a criterion in terms of which other major oral analgesics are most often measured.

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Empirin Compound with Codeine is the most widely used, and probably the most pharmaceutically elegant analgesic preparation providing codeine. It's the time-tested combination for predictable pain relief . . . whether the pain is visceral or musculoskeletal; acute or chronic.

New prescription flexibility. At your discretion, and where state law permits, a prescription for Empirin Compound with Codeine may now be refilled up to five times in six months.

Empirin Compound with Codeine No. 3 contains codeine phosphate (32.4 mg.) gr. ½. No. 4 contains codeine phosphate* (64.8 mg.) gr. 1. *(Warning—may be habit-forming.) Each tablet also contains: aspirin gr. 3½, phenacetin gr. 2½, caffeine gr. ½. Bottles of 100 and 1000.*



But for relief of Western pain

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When irritable colon feels like this



...in the presence of spasm or hypermotility, gas distension and discomfort, **KINESED®** provides more complete relief:

- ☐ **belladonna alkaloids—for the hyperactive bowel**
- ☐ **simethicone—for accompanying distension and pain due to gas**
- ☐ **phenobarbital—for associated anxiety and tension**

Composition: Each chewable, fruit-flavored, scored tablet contains: 16 mg. phenobarbital (warning: may be habit-forming); 0.1 mg. hyoscyamine sulfate; 0.02 mg. atropine sulfate; 0.007 mg. scopolamine hydrobromide; 40 mg. simethicone.
Contraindications: Hypersensitivity to barbiturates or belladonna alkaloids, glaucoma, advanced renal or hepatic disease.
Precautions: Administer with caution to patients with incipient glaucoma, bladder neck obstruction or urinary bladder atony. Prolonged use of barbiturates may be habit-forming.
Side effects: Blurred vision, dry mouth, dysuria, and other atropine-like side effects may occur at high doses, but are only rarely noted at recommended dosages.
Dosage: Adults: One or two tablets three or four times daily. Dosage can be adjusted depending on diagnosis and severity of symptoms. Children 2 to 12 years: One half or one tablet three or four times daily. Tablets may be chewed or swallowed with liquids.

STUART PHARMACEUTICALS | Pasadena, California 91109 | Division of ATLAS CHEMICAL INDUSTRIES, INC.

(from the Greek **kinetikos,**
to move,
and the Latin **sedatus,**
to calm)

KINESED®

antispasmodic/sedative/antiflatulent

Spring peeper (tree frog, *Hyla crucifer*): this small amphibian can expand its throat membrane with air until it is twice the size of its head.

Librium® (chlordiazepoxide HCl) and safety

Librium (chlordiazepoxide HCl), after more than a decade of wide clinical use, continues to reflect a wide margin of safety. In general use, the most common side effects reported have been drowsiness, ataxia and confusion, particularly in the elderly and debilitated.

Antianxiety effectiveness: Demonstrated in a broad range of psychologic and physical dysfunctions; indicated when reassurance and counseling are not enough and until, in the physician's judgment, anxiety has bee reduced to tolerable, appropriate levels.

Effect on mental acuity: Usually mini- mal on proper maintenance dosage. (See Warnings in summary of prescribing infor mation.)

Concomitant use: Is used as adjunctive antianxiety therapy concomitantly with ce tain specific medications of other classes of drugs, such as cardiac glycosides, antihype tensive agents, diuretics and vasodilators.

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in relief of clinically significant anxiety

Librium®
(chlordiazepoxide HCl)

5-mg, 10-mg, 25-mg capsules up to 100 mg daily in severe anxiety

Before prescribing, please consult complete product information, a summary of which follows:
Indications: Indicated when anxiety, tension and apprehension are significant components of the clinical profile.
Contraindications: Patients with known hypersensitivity to the drug.
Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.
Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.
Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversi ble in most instances by proper dosage adjustment, but are also occasionally ob served at the lower dosage ranges. In a few instances syncope has been reported Also encountered are isolated instances skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltag fast activity) may appear during and afte treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasion ally, making periodic blood counts and liver function tests advisable during protracted therapy.
Supplied: Librium capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.

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